A PROSPECTIVE STUDY ON MATERNAL AND FETAL OUTCOME IN JAUNDICE COMPLICATING PREGNANCY

Dissertation submitted

In partial fulfillment of requirements for

M.S. DEGREE BRANCH II

OBSTETRICS AND GYNAECOLOGY

MADRAS MEDICAL COLLEGE

CHENNAI

THE TAMILNADU DR. M.G.R.MEDICAL UNIVERSITY, CHENNAI

APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled **"A PROSPECTIVE STUDY ON MATERNAL & FETAL OUTCOME IN JAUNDICE COMPLICATING PREGNANCY"** is a bonafide work done by **DR.K.JAYANTHI** in the Institute of Obstetrics and Gynaecology (Madras Medical College) Egmore, Chennai in partial fulfillment of the university rules and regulations for award of MS degree in Obstetrics and Gynaecology under my guidance and supervision during the academic year 2011-2013.

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DECLARATION

I hereby declare that the study titled **"A PROSPECTIVE STUDY ON MATERNAL & FETAL OUTCOME IN JAUNDICE COMPLICATING PREGNANCY"** was done by me in the Institute of Obstetrics and Gynaecology (IOG), Madras Medical College, Chennai –3 during the period of my PG study for M.S Obstetrics and Gynaecology from 2011-2012 under the guidance and supervision of **Prof. Dr. D.TAMILSELVI,M.D., DGO.,**

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To

PG in MD Obstetrics & Gynaecology
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Dear Dr.

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "A Prospective study on maternal & Fetal outcome in jaundice complicating pregnancy" No.07082012.

The following members of Ethics Committee were present in the meeting held on 10/08/2012 conducted at Madras Medical College, Chennai -3.

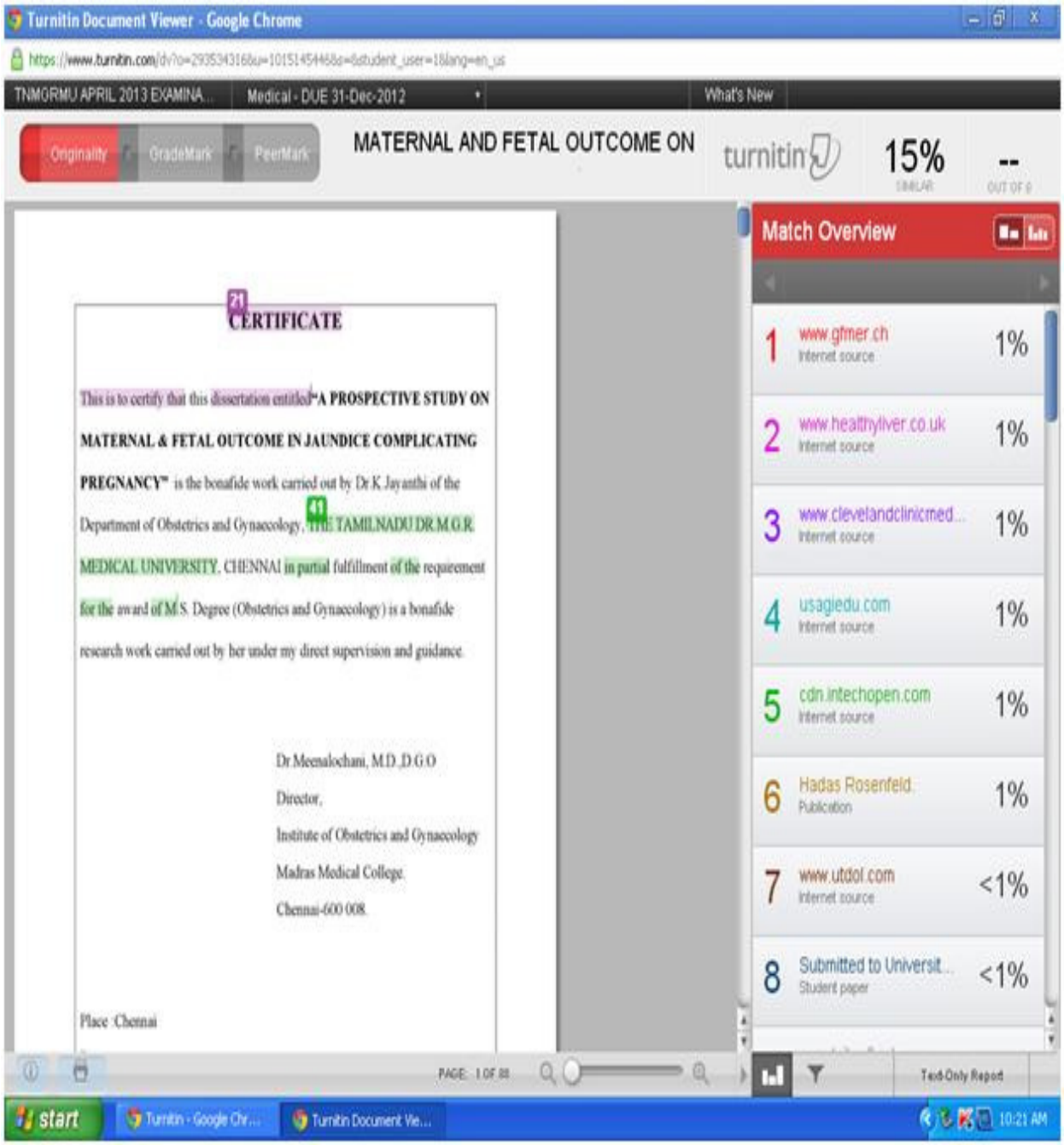
1. Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2. Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3. Prof. B. Vasanthi MD Prof of Pharmacology ,MMC, Ch-3	-- Member
4. Prof. C. Rajendiran, MD Director , Inst. Of Internal Medicine, MMC, Ch-3	-- Member
5. Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
6. Thiru. S. Govindsamy. BABL	-- Lawyer
7. Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee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INTRODUCTION

During pregnancy, the human body undergoes several changes in the process of its adaptation to the growing foetus. Although these changes are physiological, there is potential for morbidity and mortality to both mother and foetus. Liver is the site of many important metabolic and synthetic functions of the body. Abnormal liver tests occur in 3%-5% of pregnancies.

Jaundice affects a small percentage of pregnant women, yet it takes a major toll on health of both mother and foetus especially in developing countries like India. Jaundice in pregnant women has been estimated to cause 5-20% of maternal mortality and considerable percentage of perinatal wastage in India.

Liver could be the target of diseases specific to the pregnancy such as intrahepatic cholestasis of pregnancy and acute fatty liver of pregnancy, and there are no available means by which to predict with certainty how and when such illnesses may occur. In addition, morbidity is more likely in the presence of a pre-existing liver disease as in auto immune hepatitis or when a new onset liver disease occurs during pregnancy.

Acute viral hepatitis is the most common cause of jaundice in pregnancy. The outcome is usually benign. Intervention might not be required except in cases of viral hepatitis E and herpes simplex hepatitis. Pregnant women with jaundice and acute viral hepatitis caused by HEV infection has a higher maternal mortality rate and worse obstetric and fetal outcomes than did pregnant women with jaundice and acute viral hepatitis caused by other types of viral hepatitis.

Pregnancy is unusual in women with severe chronic liver disease. However, women with less severe disease or those with non cirrhotic portal hypertension do not have diminished fertility and may become pregnant.

Pregnancy has a variable effect in women with cirrhosis and portal hypertension. Worsening jaundice with progressive liver failure, ascites, and hepatic coma can occur, but some women with cirrhosis can sustain pregnancy without any worsening of hepatic function. In addition, the incidence of stillbirths and premature deliveries may be increased.

Pregnancy is generally well tolerated by women who are chronic carriers of hepatitis B virus. The overall risk of HBV transmission from the mother to infant is about 40 %. Transmission at birth is more likely if the mother is HBeAg positive or has high circulating levels of HBV

DNA. Prenatal screening of all pregnant women for HBsAg is now performed routinely in many countries. Neonates born to HBsAg positive women should receive hepatitis B immunoglobulin and HBV vaccine at birth, regardless of HBeAg status of the mother.

However, when appropriately diagnosed and managed, the outcome may be favourable and the liver disease in pregnancy could resolve without any chronic consequences. Signs and symptoms of liver disease in pregnancy are not specific, but the underlying disorder can have significant morbidity and mortality effects on the mother and foetus. Early recognition can be lifesaving.

Vigilance in recognizing liver disorders in pregnancy and early coordinated management among the primary care physician, obstetrician, and liver specialist are essential for promoting good maternal and fetal outcomes.

Therefore this study is undertaken in Institute of Obstetrics and Gynaecology with an aim to analyse the cause of the disease, altered liver function, maternal and fetal morbidity and mortality and preventive measures. This study will help in better understanding and improving the maternal and perinatal outcome in jaundice complicating pregnancy.

AIMS AND OBJECTIVE

- To evaluate the etiology of jaundice complicating pregnancy in patients of Institute of Obstetrics and Gynaecology.
- To evaluate the maternal and fetal outcome of jaundice complicating pregnancy.
- To evaluate the efficacy of prophylactic measures in the prevention of jaundice.

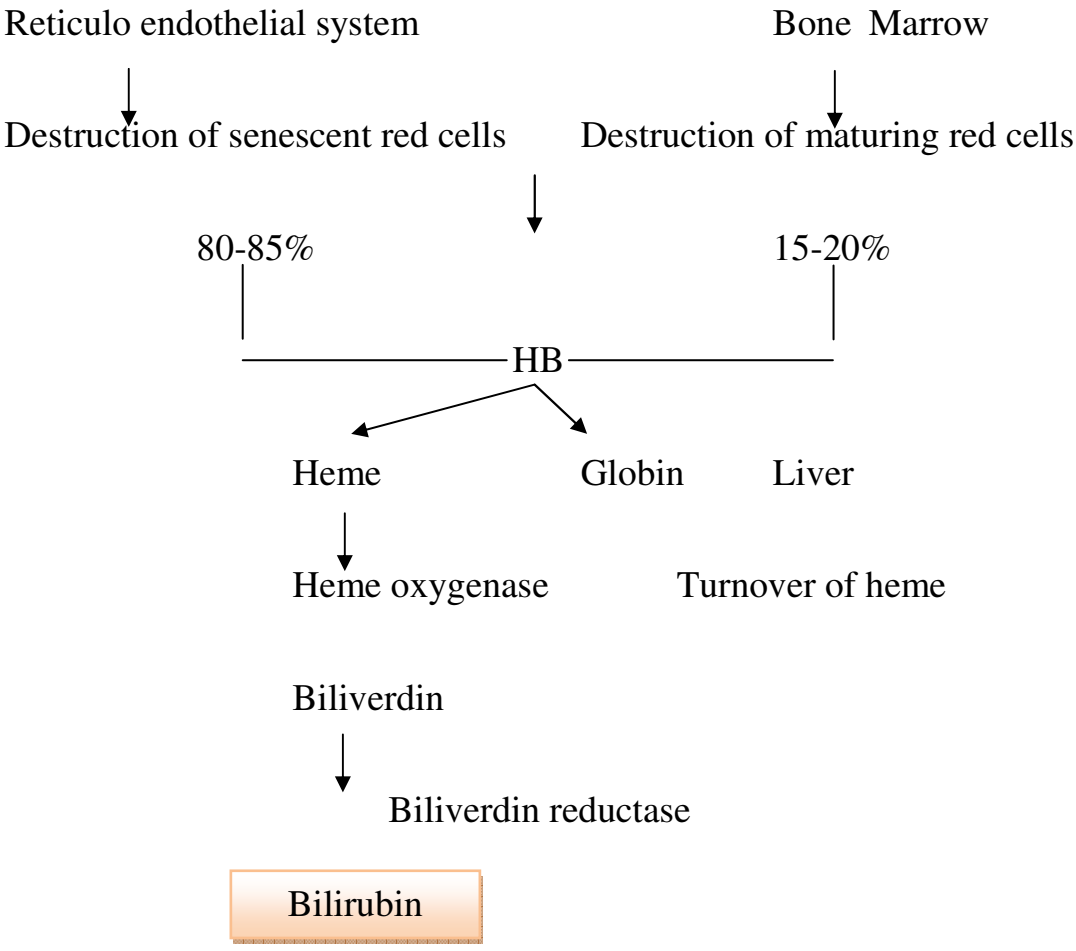
REVIEW OF LITERATURE

CONCEPTS OF JAUNDICE

Jaundice is the yellowish staining of the skin and sclera that is caused by high levels bilirubin in blood . Total value above 2.5 mg/dl of bilirubin is associated with clinical jaundice.

Production & metabolism of bilirubin:

Source of bilirubin:



Unconjugated form is bound tightly to albumin in plasma

Hepatic metabolism of Bilirubin:

Three phases 1. Hepatic uptake

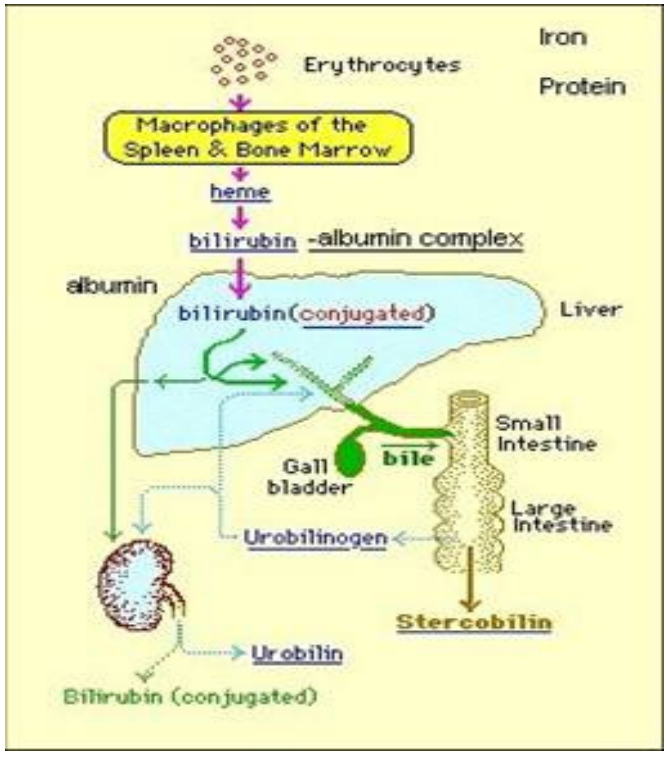
2. Conjugation

3. Excretion into bile -rate limiting step

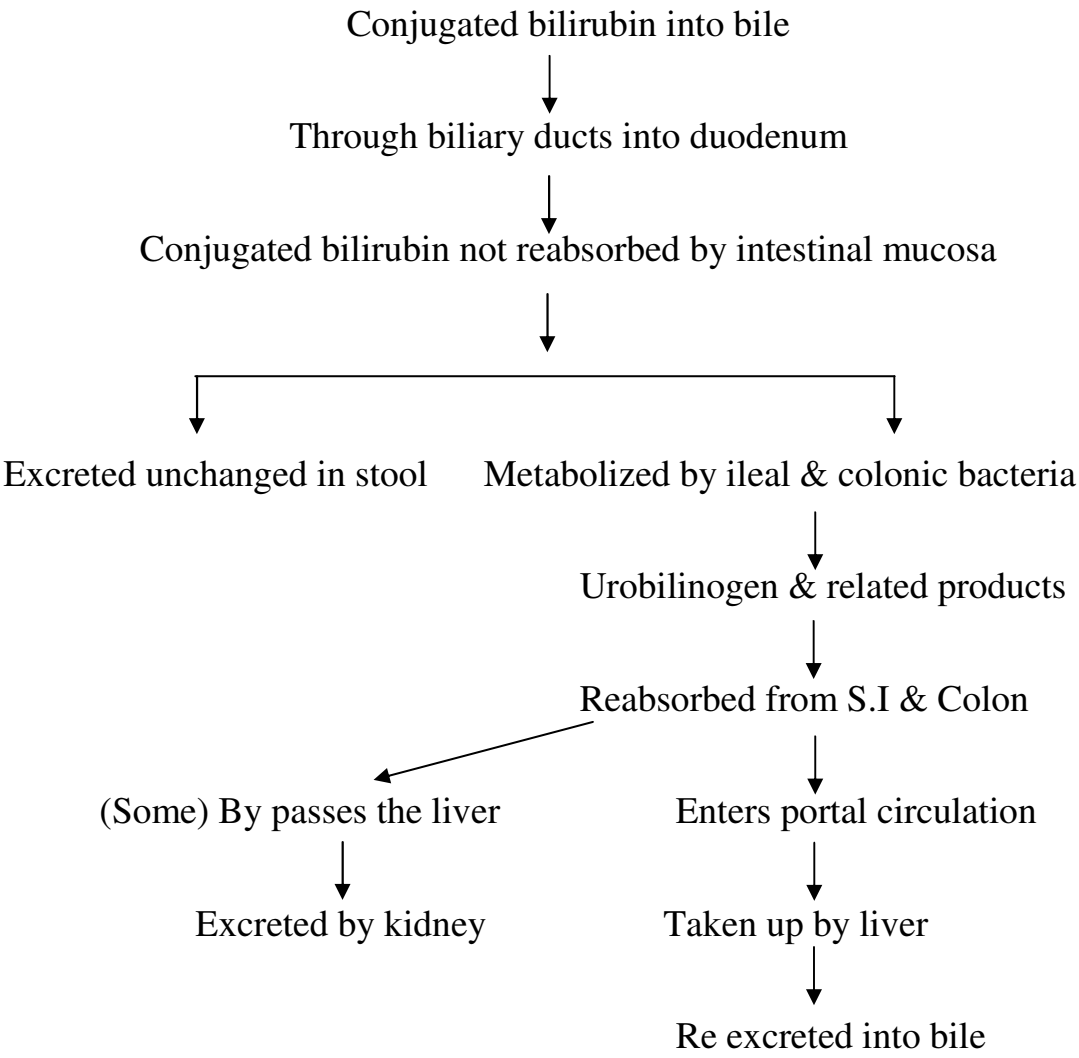
Uptake and Conjugation:

Unconjugated bilirubin bound to albumin enters liver and the complex dissociates. Non-polar bilirubin enters the hepatocyte and gets conjugated to glucuronic acid forming bilirubin glucuronide, which is water-soluble. Only conjugated bilirubin can be excreted into bile.

BILIRUBIN METABOLISM



Intestinal phase of bilirubin metabolism:



Normal daily urinary excretion of urobilinogen does not exceed 4mg.

Increased Excretion of Urobilinogen – Due to:

1. Hepatic uptake & excretion is impaired in hepatocellular disease.
2. Increase bilirubin production as in hemolysis.

Decrease Excretion of Urobilinogen – Due to:

Cholestasis

Extra hepatic biliary obstruction

Renal excretion of bilirubin:

Normally there is no detectable bilirubin in urine. Only conjugated bilirubin can be excreted. Bile salts enhance glomerular filtration of conjugated bilirubin.

In cholestasis & extra hepatic biliary obstruction there is increasing circulating bile salts and increase in bilirubin excretion.

Differential diagnosis of jaundice

	Prehepatic	Intrahepatic	Posthepatic
conjugated bilirubin	absent	↑	↑
AST or ALT	normal	↑	normal
ALP	normal	normal	↑
urine bilirubin	absent	present	present
urine urobilinogen	present	present	absent

IMPORTANT FUNCTIONS OF THE LIVER

Bilirubin metabolism

Bile acid metabolism

Carbohydrate metabolism

Lipid metabolism

Xenobiotic metabolism

Protein synthesis

Immune function

Changes in Liver During Pregnancy:

Anatomical changes:

No alteration in liver weight occurs. During III Trimester, liver occupies more postero superior position with displacement to right and reduction in dullness to percussion.

Hence detection of hepatomegaly is a strong evidence for the presence of liver disease.

Physiological Changes

Hepatic blood flow is maintained in pregnancy unaltered, resulting in a decline in the proportion of cardiac output delivered to liver by 35%. This is due to increase in plasma and blood volume by 50% and rise in cardiac output by 50%.

The relative decrease in hepatic blood flow may contribute to reduction in clearance of various compounds from blood.

Protein metabolism: Synthesis of all serum proteins is affected. Total serum protein concentration is decreased by 20% primarily due to fall in S.albumin. This is due to

1. Hemo dilution
2. Increase in albumin catabolism.

Serum α1, α2, β globulins – rise up to 50%.

Bilirubin metabolism:

Slight rise in S.bilirubin in 5% pregnancy otherwise normal is reported, due to increased bile viscosity & histologically dilated biliary canaliculi.

Increase in S.bilirubin in pregnancy should be considered as presumptive evidence for presence of liver or hematological disorder.

Serum enzymes:

Total S.alkaline phosphatase is elevated more in III trimester, increases by 2-4 times normal, major source being placenta.

Gamma glutaryl transpeptidase, LDH are increased near term.

SGOT & SGPT:

They are only slightly altered by normal pregnancy. May rise near term, but within normal range**.**

Physical examination — Spider angiomas and palmar erythema, which are classically associated with chronic liver disease, are also common during pregnancy and usually disappear after delivery. It is presumed that the hyperestrogenemia of pregnancy is responsible for these changes.

LIVER FUNCTION TESTS

In a case of jaundice complicating pregnancy, liver function tests is done to

- confirm the diagnosis
- assess the severity of the disease
- assess the prognosis

TESTS OF BILIARY EXCRETION

1. **Serum Bilirubin**:Vandenberg's method (1913) of spectrophotometric determination is used.

   Normal values are Total: 0.3-1 mg/ dl

   Direct: 0.25 mg %(Conjugated bilirubin)

   Indirect: 0.75mg %(unconjugated bilirubin)

   If indirect bilirubin is more than 80% of total bilirubin, it is called predominantly unconjugated hyperbilirubinemia**.**

   If direct bilirubin is more than 50% of total bilirubin, it is called predominantly conjugated hyperbilirubinemia

2. **Urine bilirubin (Bile Pigments)**

   This is estimated by modified **fouchet's test &Hay's test.** Bilirubinuria occurs when there is an increase in the serum conjugated bilirubin. So it is absent in hemolytic jaundice. Bilirubinuria occurs even with minimal liver damage and can be detected even before clinical manifestation.

3. **Urine urobilinogen**

   It is detected by **Ehrlichs Aldehyde test**

   It is strongly positive in hemolytic jaundice.

   In viral hepatitis, it is positive during preicteric and convalescent phase but disappears during icteric phase.

II. TESTS OF METABOLIC FUNCTION

1. Serum proteins: Serum proteins are estimated by precipitation of globulin with 23% sodium sulphate. The remaining protein in solution is taken as albumin. The normal serum proteins are Total: 6-8.5 gm/dl and globulin2.4-3.7 g/dl. Normal Albumin- Globulin ratio is 1.5.

In diffuse parenchymal liver diseases albumin concentration falls and globulin fraction increases relatively. The albumin globulin ratio is reversed in such conditions.

2. Serum alkaline phosphatase: Normal value is 5-15 KA units. It is synthesized by liver, bone, intestine, placenta, etc. So to be specific, electrophoretic separation of isoenzymes of alkaline phosphatase is to be done. Marked rise occurs both in intrahepatic and extra hepatic cholestasis.

Clotting factors

Liver synthesizes the clotting **factors II,V,VII,IX&X. S**o in the presence of severe hepatocellular damage,

1. Clotting time is prolonged (Normal 5-15 minutes).

2. Prothrombin time is increased, It measure the factors involved in the 2^{nd} and 3^{rd} stages of coagulation in extrinsic coagulation system.

III. TESTS OF LIVER CELL DAMAGE

1. Serum Glutamic- pyruvic transaminases (SGPT or ALT)

SGPT is specifically associated with the liver parenchymal cells and released into the plasma in large amounts when the liver cells are damaged. Normal level of SGPT 5-35 IU/L.

2. Serum Glutamic-Oxaloacetic transaminases (SGPT or AST)

SGPT is associated with the liver, brain and heart tissues and released into the plasma in large amounts when these organs are damaged Normal level of SGOT : 5-40 IU/L.

3. Serum Gamma Glutamyltransferase (SGGT)

SGGT is associated with Alcoholism or Biliary stasis.

With parenchymal liver diseases, the aminotransferase enzymes are elevated sometimes to several hundreds. So estimation is needed for follow-up. In patients with **acute fulminant hepatitis**, serum aminotransferase **may decrease** due to previous excessive release of these enzymes and this is the omnious sign.

CLASSIFICATION OF JAUNDICE IN PREGNANCY

Jaundice peculiar to pregnancy

• Hyperemesis gravidarum

• Intrahepatic cholestasis of pregnancy

• HELLP syndrome

• Acute fatty liver of pregnancy

Jaundice superimposed on pregnancy

• Viral hepatitis

• Gall stone

• Drug-induced hepatotoxicity

• Haemolytic jaundice

Pregnancy superimposed on liver diseases

•Cirrhosis and portal hypertension

•Wilson's disease

•Hepatitis B and C

•Autoimmune liver disease

JAUNDICE SUPERIMPOSED ON PREGNANCY

CAUSES OF VIRAL HEPATITIS

- Hepatitis A Virus
- Hepatitis B Virus
- Hepatitis C Virus
- Hepatitis D Virus
- Hepatitis E Virus

Other uncommon viruses

- Herpes simplex virus
- Cytomegalovirus
- Epstein Barr virus
- Yellow fever virus

Bacterial diseases

- Leptospirosis
- Typhoid fever
- Gonococcal disease

Parasites

- Malaria

FEATURES OF THE MAIN HEPATITIS VIRUSES

	Hepatitis A	**HepatitisB**	**Hepatitis C**	**Hepatitis D**	**Hepatitis E**
Virus Group/ Nucleic Acid/ Size(diameter)	Enterovirus RNA 27nm	Hepadno DNA 42nm	Flavi virus RNA 30-38nm	Incomplete RNA 35nm	Calci virus RNA 27nm
Incubation period(weeks)	2-4	4-20	2-26	6-9	3-8
Seasonal Incidence	Winter	Year around	Year around	Year around	Winter
Age	Children	Any	Any	Any	Any
Spread 1. Feco-oral 2. Blood 3. Sexual 4. vertical	Yes Uncommon Uncommon No	No Yes Yes Yes	No Yes Uncommon Uncommon	No Yes Yes Yes	Yes No ? No
Type of onset	Acute	Insidious	Insidious	Acute or Insidious	Acute
Fever	common	Less common	Less common	Less common	common
Carrier state	No	Yes (5-10%)	Yes>50%	Yes	No
Prognosis	Good	Worse with Age	Moderate	Same as HBV	Good except In pregnancy
Prevention Active Passive	Vaccine immune serum globulin	Vaccine Hyper immune Serum globulin	 No No	Prevented by Prevention of Hepatitis B Virus infection	Under trial

Clinical features of viral Hepatitis

- **Preicteric period**
  - In Hepatitis A and Hepatitis E the onset is abrupt with fever but in Hepatitis B and Hepatitis C the onset is insidious.
  - The initial symptoms are loss of appetite, nausea, vomiting, lassitude, abdominal pain and diarrhea.
  - At the end of the period, the urine darkens.
  - The duration of this period varies from 1-21 days, average 5-7 days.
- **Icteric period**
  - The urine deepens continuously and jaundice appears on the skin and sclera within 2 weeks.
  - Subjective symptoms abate.
  - Liver palpable in7%, spleen palpable in 20%.
  - The period lasts for 2-6 weeks.
- **Convalescent period**
  - The jaundice disappears gradually.
  - Liver and spleen retract, liver function return to normal.
  - The period lasts 2 weeks to 4 months, average 1 month.
  - About 10% of Hepatitis B and 50% of Hepatitis C will become chronic hepatitis.
  - Acute hepatitis E is similar to acute hepatitis A, but cholestasis is obvious and symptoms and signs are severe.

Fulminant Hepatitis

Development of hepatic encephalopathy within 8 weeks of initiation of symptoms in a patient without known chronic liver disease.

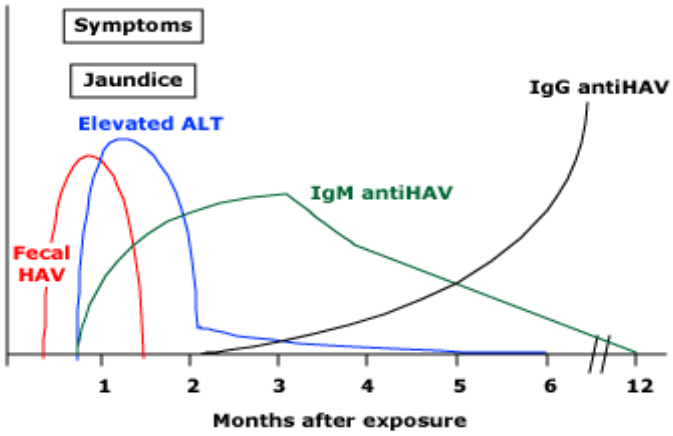
All five kinds of hepatitis virus can cause this type of hepatitis. The incidence is only 0.2-0.5%, but the mortality is high.

- The onset may begin in a typical acute icteric hepatitis, but within 10 days
- Jaundice deepens rapidly
- Vomit is frequent
- Obvious anorexia
- Hemorrhage
- The liver shrinks in size with massive necrosis.
- Prothrombin time is prolonged
- Ascites appear
- Acute renal failure
- Hepatic encephalopathy

HEPATITIS A

Hepatitis A spread via the feco-oral route, and common in low socioeconomic areas. The hepatitis A infection during pregnancy is similar to that in nonpregnant patients.But gestational complications are common.[1]Vertical transmission has not been reported. Sexual and household contact with hepatitis A is reported in about 10 % of cases.[2]

Course of hepatitis A



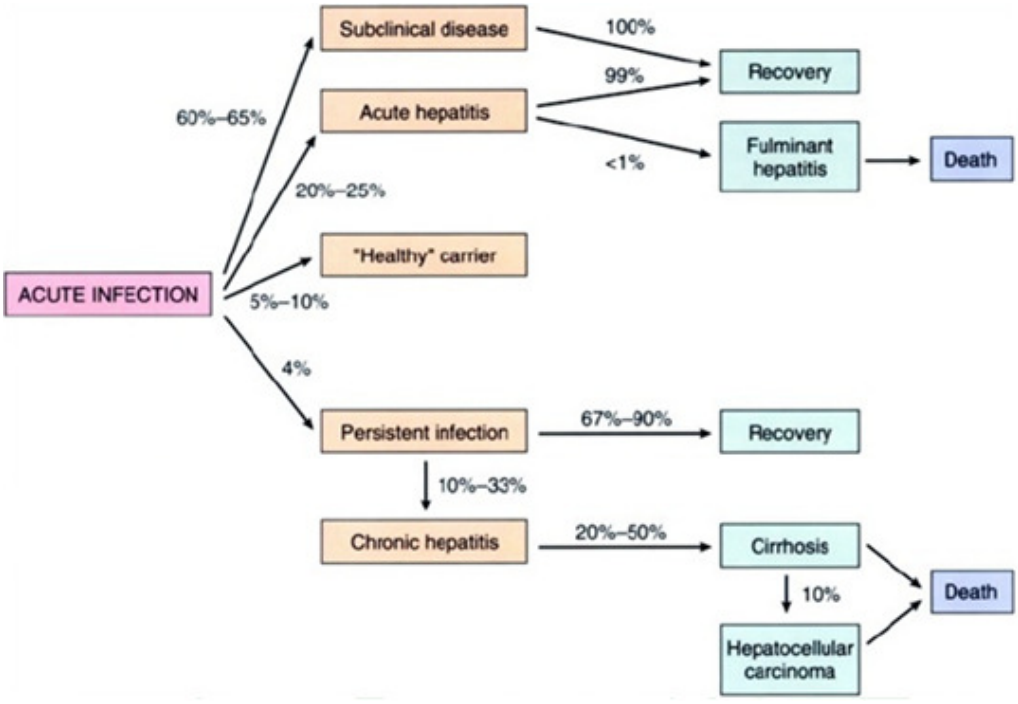
DIAGNOSIS — Acute HAV infection is detected by anti-HAV antibodies. It is seen at the onset of symptoms, peaks during the acute or early convalescent period, and it is present for 4 to 6months.IgG anti-HAV is detected early in the convalescent phase, and remains for years.

TREATMENT—As the disease is self-limited, the treatment is symptomatic and supportive.

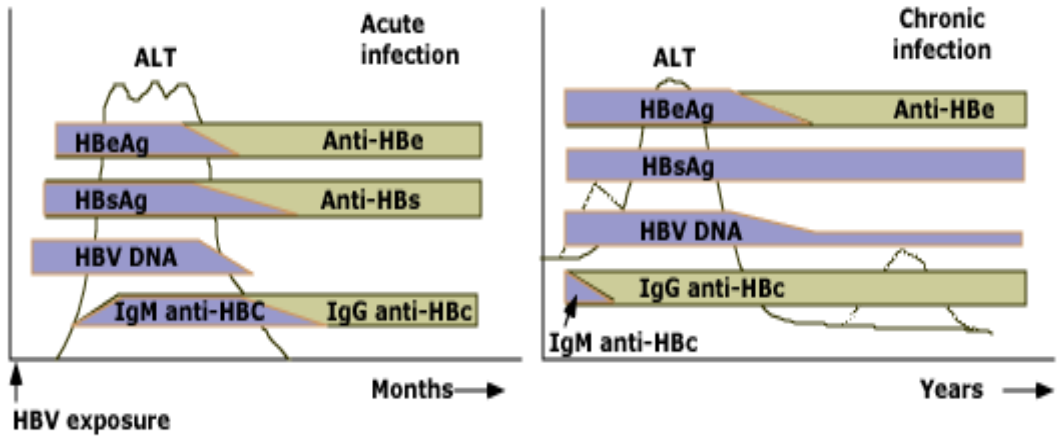
PREVENTION — Prevention is by proper hand washing, and drinking safe water. Chlorination inactivates the virus. Immunoglobulin (IG) prevents 80%-90% of cases of hepatitis A if it is given shortly after the infection or before exposure.[3]

HEPATITIS B

Acute HBV infection do not increases mortality during pregnancy and it has no teratogenic effects. However, a higher incidence of low birth weight and prematurity has been reported. About 350 million individuals are chronically infected with hepatitis B virus (HBV) worldwide, and at least 50% of them acquired their infections either perinatally or in early childhood. Hence prevention of perinatal transmission is a high priority to decrease the global burden of chronic HBV.



COURSE OF HEPATITIS B



Acute infection is characterized initially by the presence of HBeAg. HBsAg and HBV DNA begins in the preclinical phase. IgM anti-HBc appears early in the clinical phase, the combination of IgM anti-HBc and HBsAg makes the diagnosis of acute infection. Recovery is accompanied by normalization of the serum ALT, the disappearance of HBV DNA, HBeAg to anti-HBe seroconversion, and subsequently HBsAg to anti-HBs seroconversion and switch from IgM to IgG anti-HBc.

Chronic infection is characterized by persistence of HBeAg (for a variable period), HBsAg, and HBV DNA in the circulation; anti-HBs is not seen. Persistence of HBsAg for more than six months after acute infection is considered indicative of chronic infection.

Interpretation of serology tests for hepatitis B.[4]

Test	Acute Hepatitis B	Immunity following infection	Immunity due to vaccination	Chronic Hepatitis B — Active	Chronic Hepatitis B— Inactive Carrier
HBsAg	+	–	–	+	+
Anti-HBs	–	+	+	–	–
HBeAg	+	–	–	+/–	–
Anti-HBe	–	+/–	–	+/–	+
Anti-HBc	+	+	–	+	+
IgM anti-HBc	+	–	–	–	–
HBV DNA	+	–	–	+	+ (low)
ALT	Elevated	Normal	Normal	Elevated	Normal

HBV Transmission[5]

In utero (<10%)

Associated with

- Acute HBV in third trimester
- Maternal HBeAg and high HBV DNA
- History of threatened preterm labor

At the time of delivery

- HBeAg-positive mothers: 85%
- HBeAg-negative mothers: 31%
- caesarean section does not prevent transmission

After birth

- Breastfeeding not associated with transmission

Risk of perinatal transmission[6]

	Without immunoprophylaxis	HBIG and HBV vaccine series
HBeAg positive	70-90%	5-10%
HBeAg negative	10-40%	<5%

Post Exposure Prophylaxis (PEP):

- Dose 1 of Hep B vaccine in the thigh within 12 hrs of birth and HBIG 0.5 ml in the opposite thigh IM within 12 hrs of birth but not later than 7 days.
- Dose 2 of hepatitis B vaccine at 1-2 months of age. Dose 3 of hepatitis B vaccine at 6 months of age. The Infant < 2000 gms should receive a total of 4 hep B doses .(Liver International 2009; 29 : 135 -139)

- Active plus passive immunization is 95% effective and only Active immunization is 72% effective in preventing transmission.
- Lamivudine 100mg /day given 1 month before delivery decreases HBV transmission from 28.0% to 12.5% .[7]
- Post-vaccination testing (PVT) should be done in all infants after the third dose of hepatitis B vaccine ideally at the 9 or 12 month visit.
- 90% of infected infants become chronic carriers in the absence of post exposure prophylaxis.

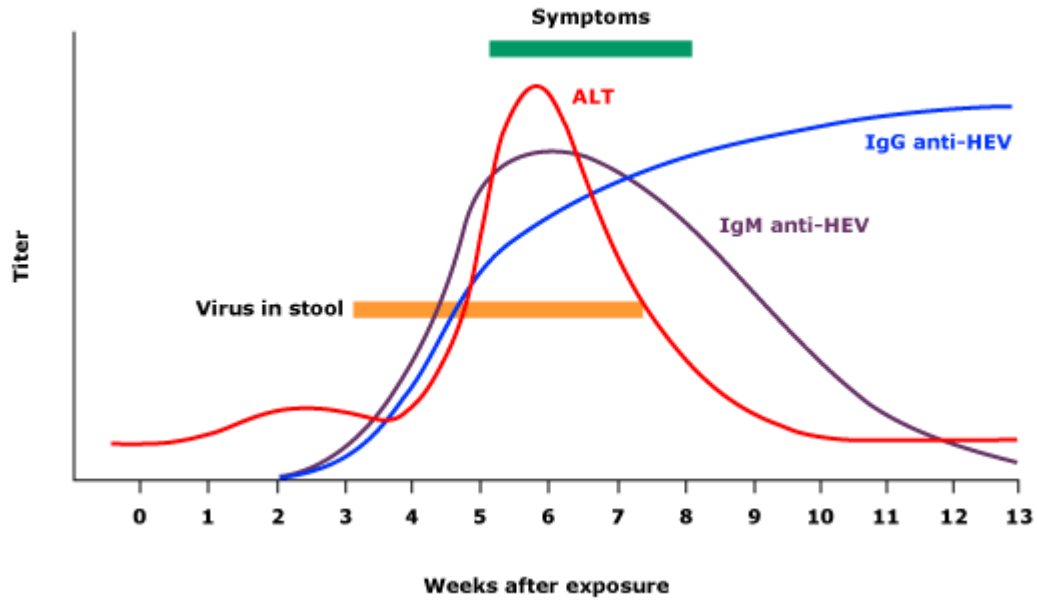
Hence, all antenatal patients should be screened universally for Hepatitis B and babies of positive mothers should receive both Active and Passive immunization.

HEPATITIS E

Hepatitis E virus (HEV) is transmitted feco-orally. Infection with Hepatitis E was first reported in 1955 in New Delhi, India.[8] Some patients have asymptomatic infection .Hepatitis E is more severe compared with hepatitis A especially in pregnant women.

DIAGNOSIS — Acute infection is diagnosed by the presence of of IgM HEV antibodies in serum. Hepatitis E virus is detected in serum or stool by Polymerase chain reaction (PCR).Antibody tests against HEV are often associated with false positive and negative results.

Course of hepatitis E



The incubation period after oral exposure is four to five weeks. HEV can be detected in stool one week before the onset of illness and it is present for two weeks. Because HEV is enterically transmitted, patients are infectious during fecal shedding. While HEV viremia is short-lived in most patients, it can persist for up to four months.

IgM anti-HEV appears during early phase of clinical illness and disappears rapidly over four to five months. The IgG antibodies appears shortly after the IgM, remaining high from 1 to as long as 14 years.[9]

PREGNANCY

Hepatitis E infection results in fulminant hepatic failure and high mortality in 15 - 25 %pregnant women. Pregnancy with an altered status of sex

steroid hormones and reduced immunocompetence predisposes to increased viral replication [10]. They have poor obstetric and fetal outcomes when compared with other viral hepatitis.

Breastfeeding is not contraindicated.

PREVENTION AND TREATMENT

Prevention is by proper hand washing and drinking safe water. Vaccines against HEV are in development. Two large placebo-controlled trials found that vaccination was more than 96 percent effective in preventing infection in high-risk settings. Pre- or Post-exposure immune globulin (IG) for prophylaxis of Hepatitis E infection is under trial.[11]

HEPATITIS C

Women chronically infected with hepatitis C virus (HCV) can have an uneventful pregnancy without worsening of liver disease or other adverse effects on the mother or fetus, though some studies have suggested potential harms. Transmission of the virus from mother to infant occurs but appears to be much less efficient than for hepatitis B, occurring in about 5 to 10 % of infants born to anti-HCV positive women. Antiviral treatment of pregnant women with hepatitis C or unusual precautions to reduce the risk of transmission (performing a cesarean delivery) are not recommended.

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

It is the most common condition peculiar to pregnancy, has a mild course in mother but an adverse effect on fetus. Geographical variation in incidence is wide, there is a seasonal variation peaking in November, have familial predisposition and tends to recur. (17)

Etiopathogenesis:

It is a multifactorial disease. Exact etiology is not known. Increased sex hormone synthesis and metabolism during pregnancy may be one of the factors.

- Genetic factors may play a role. [12]Pauli Magnus et al 2006 studied that "The ABCB4 (adenosine triphosphate-binding cassette, subfamily B, member 4) gene encoding the multidrug resistance 3 (MDR3) protein (a canalicular phospholipid translocator) is primarily involved in a subtype of progressive familial intrahepatic cholestasis called PFIC3. Heterozygous mutations in this gene have been found in women who had episodes of cholestasis during pregnancy. The prevalence of such ABCB4 gene mutations in Caucasian patients suffering from ICP is 16 percent."[13]

- Role of estrogen & progesterone.[14]
- Higher incidence in twin gestation favors ICP.[15]
- Low s. selenium levels reduce the activity of some selenium dependent liver enzymes.

Diagnosis:

80% of cases usually occur in III trimesters of pregnancy. Generalized pruritus occurs after 30th week, relieved within 48 hours following delivery. They have mild jaundice, 2-4 weeks after the onset of pruritus. Nocturnal itching of trunk, palms and soles is severe along with insomnia and fatigue.

Biochemical changes:

There is rise in serum bile acids & mild elevation in S.transaminase and S.bilirubin level as shown in tabular column.

Parameters	Change
S. bile acids	10-100 fold
S. alkaline Phosphatase	7-10 fold
S. bilirubin	2-5
5' nucleotidase	2 fold
PT time	N-2 fold
Cholesterol	2-4 fold
TG	N-2 fold

Effects on mother are pruritus, PPH and gallstones.

FETAL OUTCOME

Effects on fetus are prematurity, respiratory distress syndrome, meconium staining and fetal death. Williamson et al 2011states that

"The incidence of prematurity varies greatly among studies (6 to 60 percent), and may be related to the sudden development of a fetal arrhythmia or vasospasm of the placental chorionic surface vessels induced by high levels of bile acids".[16] Maternal serum bile acid concentration also is a predictor of fetal outcome risk in cholestasis of pregnancy.[17]

MANAGEMENT

- Treatment is symptomatic and supportive.
- Ursodeoxycholic acid 500mg BD or 300mg TDS relieves pruritus by increasing bile flow and and also improves the liver function tests. [18, 19]
- Cholestyramine acts by reducing the ileal absorption of bile salts, so that their fecal excretion is increased. The dose of Cholestyramine is 4gm four times a day.
- Antihistamines can be given to relieve intense pruritus.
- Frequent fetal monitoring by Non stress test. Delivery at 37 weeks as the risk of intra uterine death is more after 37 weeks.

ACUTE FATTY LIVER OF PREGNANCY

Stander and Carden recognized AFLP in 1940 and this liver disorder is unique to human. It occurs in the third trimester and is more common with multiple gestations.

CLINICAL MANIFESTATIONS

Acute fatty liver occurs typically in the third trimester. The disease is always present before delivery, although not always diagnosed prior to delivery.

The symptoms are nausea or vomiting (75 %),abdominal pain (particularly epigastric 50%), loss of appetite and jaundice. About 50% have signs of preeclampsia. [20].

PATHOGENESIS — The relation of AFLP with the inherited defects in mitochondrial beta-oxidation of fatty acids and long-chain 3-hydroxyacyl CoA dehydrogenase deficiency (LCHAD) had shown that some affected patients and their fetus have an inherited enzyme deficiency in beta-oxidation. [21] These metabolites produced by the fetus or placenta are toxic to the liver resulting in liver disease. The role of LCHAD in the pathogenesis of acute fatty liver of pregnancy has been illustrated in many studies and is common in male fetus.

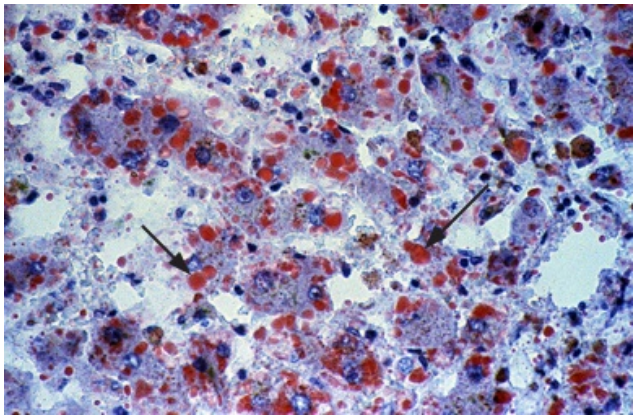
Swansea diagnostic criteria for AFLP (Six or more features)

- Vomiting
- Abdominal pain
- Polydipsia and polyuria
- Elevated transaminases(3 to 10times)
- Encephalopathy
- High bilirubin (>14 μmol/L)
- Hypoglycaemia (<4 mmol/L)
- Elevated urate (>340 μmol/L
- Renal impairment (creatinine>150 μmol/L)
- Leucocytosis (>11×109/L)
- Ascites or bright liver on ultrasound scan
- Elevated ammonia (>47 μmol/L)
- Coagulopathy (PT >14 sec or APTT >34 sec)
- Liver biopsy showing micro vesicular steatosis

DIAGNOSIS — AFLP is mostly diagnosed clinically and with laboratory and imaging results.

Liver biopsy is diagnostic, showing the characteristic picture of the micro vesicular fatty infiltration of the hepatocytes. Because liver biopsy is invasive, it is not always performed. Liver biopsy should be approached with caution during pregnancy, and reserved for cases in which the diagnosis is in doubt.

Acute fatty liver of pregnancy



High power view of an oil red O stain of a liver biopsy of acute fatty liver. There are vacuolated hepatocytes containing micro vesicular fat which stain red (arrows) Courtesy of Caroline ARiely, MD.

TREATMENT AND COURSE — There is no specific medical treatment for AFLP.The primary treatment is prompt delivery of the fetus after maternal stabilization.

Hypoglycemia is common and treated with a continuous infusion of 10 percent dextrose solution. Coagulopathy is treated with fresh frozen plasma, packed red blood cells, cryoprecipitate and platelets. Severe cases require intensive care unit with mechanical ventilation. However, substantial morbidity and mortality can occur. [22]

HELLP SYNDROME

HELLP syndrome is characterized by microangiopathic haemolytic anaemia, raised liver enzymes, and reduced platelet count.

Partial HELLP syndrome: Patients with one or two criteria of HELLP syndrome.

INCIDENCE—The incidence of HELLP syndrome is 1 - 2 per 1000 pregnancies and is seen in 15 to 20 percent of women with severe preeclampsia/eclampsia. Most of the patients are between 28 and 36 weeks of gestation. [23]

Signs/symptoms

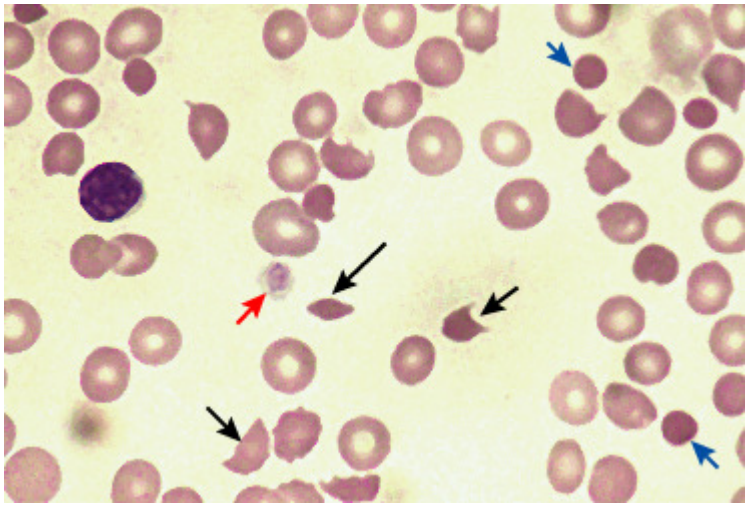
Proteinuria	Right upper quadrant/epigastric pain
Hypertension	Nausea, vomiting
Headache	Visual changes
Jaundice	

Hypertension and proteinuria are seen in 85% patients.

DIAGNOSIS

1. Microangiopathic haemolytic anemia with schistocytes (also known as helmet cells) on blood smears. Other features of hemolysis are raised indirect bilirubin and a low serum haptoglobin.
2. Platelet count ≤ 1 lakh
3. Total bilirubin ≥1.2 mg/dL
4. Serum AST ≥70 IU/L

Peripheral smear in microangiopathic haemolytic anemia showing presence of schistocytes.



Peripheral smear with microangiopathic haemolytic anemia. Helmet cells (small black arrows), fragmented red cells (large black arrow), microspherocytes (blue arrows). The platelet number is reduced (red arrow) showing enhanced destruction. Courtesy of Carola von Kapff, SH (ASCP).

Differential diagnosis — Acute fatty liver of pregnancy, Gallbladder disease, Idiopathic thrombocytopenic purpura, Hemolytic-uremic syndrome and Thrombotic thrombocytopenic purpura.

Classificationof HELLP syndrome

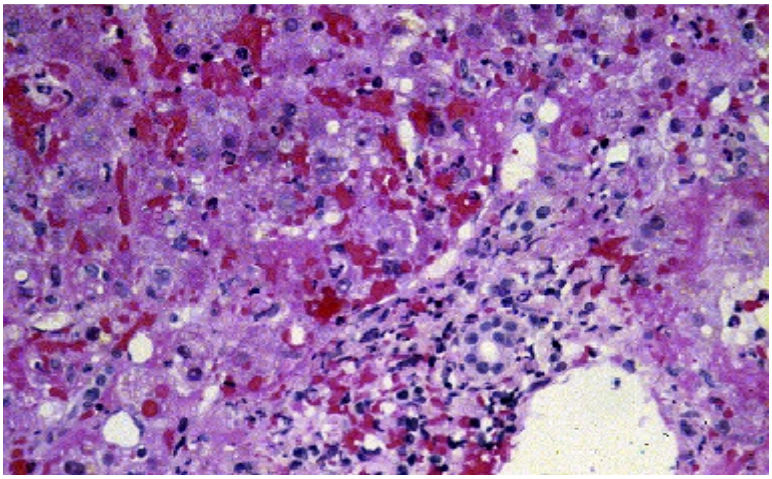
Mississippi system

• Class I: platelets <50,000/mm3

• Class II: platelets 50,000-1,00,000/mm3

• Class III: platelets 100,000-1,50,000/mm3

AST>40 IU/L and LDH >600 IU/L



Liver biopsy from a patient with HELLP syndrome. The zones immediately adjacent to the portal triads show collections of red blood cells, without inflammation or necrosis of hepatocytes. Courtesy of Caroline A Riely, MD.

MANAGEMENT

The cornerstone of therapy is delivery. Antihypertensives are used for treating severe hypertension. Magnesium sulfate is given intravenously to prevent convulsions.

Pregnancies less than 34 weeks of gestation: There is no evidence that perinatal outcome is improved with expectant management when compared with fetus delivered after a course of glucocorticoids. There are no maternal benefits from expectant management. [24].

Role of dexamethasone: Some recommend use of dexamethasone in patients with platelet counts less than 100,000. Cochrane review of 11 trials comparing corticosteroids with placebo in women with HELLP syndrome found no difference in maternal death, maternal morbidity, or perinatal death and concluded there was no clear evidence of benefit.[25]

Complications

DIC 21%

Abruptio placentae 16%

Acute renal failure 8 %

Pulmonary edema 6%

Subcapsular liver hematoma 1%

Retinal detachment 1%

Fetal/neonatal long-term prognosis are most strongly associated with gestational age at delivery and birth weight. Prematurity is common (70 percent), and may be complicated by intrauterine growth restriction and sequelae of abruptio placenta.[26]

Biochemical differences between AFLP and HELLP

	AFLP	**HELLP**
Glucose	low	Normal
Ammonia	High	Normal
RBC	Normal	Hemolysis
Platelet in	low to Normal	Low
Fibrinogen	Low	Normal
Prothrombin time	prolonged	Normal

CHRONIC LIVER DISEASE AND PORTAL HYPERTENSION

Pregnancy is unusual in women with severe chronic liver disease because of the associated anovulatory state. But women with less severe disease (chronic viral hepatitis) or those with non cirrhotic portal hypertension

(portal vein thrombosis) do not have diminished fertility and may become pregnant.[27]

The increase in total blood volume associated with pregnancy may worsen pre-existing portal hypertension .The maternal complications of portal hypertension are variceal haemorrhage , encephalopathy, hepatic failure, jaundice, malnutrition , and the fetal complications are stillbirths and premature delivery.

Esophageal variceal bleeding is more common during the second and third trimesters due to increased pressure of the expanding uterus on the inferior vena cava. Maternal mortality with acute variceal bleeds ranges from 20-50%.[27]

Upper endoscopy should be performed in the second trimester for all pregnant women with portal hypertension. Patients at high risk for variceal hemorrhage should be considered for sclerotherapy. Prophylaxis with beta blockers, propranolol may be continued during pregnancy, but newborns should be monitored during the first days of life because of risks of hypoglycemia and bradycardia.[28]

Vaginal delivery is usually safe and early forceps delivery or vacuum extraction should be considered to prevent any rise in portal pressure due to prolonged straining during labour [29].

Other chronic liver disorders are Wilsons disease, Budd-Chiari syndrome, autoimmune hepatitis (Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis).

GALLSTONES

Gallstones are common in pregnancy due to increased cholesterol secretion, increased lithogenicity of the bile, and reduced gallbladder motility.

By the third trimester10% of pregnant women have gallstones. Most gallstones regress in the postpartum period.

The treatment may be conservative or surgical, depending on the severity of the symptoms. Laparoscopic cholecystectomy can be done for symptomatic gallstones in pregnancy.[30]Endoscopic retrograde cholangiopancreatography (ERCP) may be needed for choledocholithiasis.

HEREDITARY SPHEROCYTOSIS

Hereditary spherocytosis is an autosomal dominant hematologic disorder. It also occur as an autosomal recessive disorder with variable expression.

Clinical features Hemolytic anemia (of varying severity) with spherocytosis, intermittent jaundice, splenomegaly, and gall stones.

Diagnostic criteria

Red cell indices: Hb, MCV are decreased, MCHC, RDW, reticulocyte count are increased. Osmotic fragility is increased. Blood smear shows spherocytes. Direct antiglobulin test is negative.

Mild form of Hereditary spherocytosis do not have major problems. Hemolytic crisis is common during pregnancy. Few cases are diagnosed only during pregnancy.

Symptomatic patients should undergo splenectomy to prevent hemolytic crisis in pregnancy [31]

HERPES SIMPLEX HEPATITIS IN PREGNANCY

- Predominant in pregnant women.
- Virus is herpes simplex type 2.
- S.bilirubin is mildly elevated but S.transaminase is markedly elevated.
- Maternal and fetal mortality is about 50%.
- Acyclovir is the treatment of choice.

HYPEREMESIS GRAVIDARUM

The incidence of Hyperemesis in pregnancy is about 0.5 to 2 percent.It is characterised by intractable nausea and vomiting and it is common in primigravida.It may cause in mild elevation of bilirubin and liver enzymes along with metabolic disturbances. Treatment is hydration and antiemetics.

According to Matsubra.S et al "In women with Jaundice in hyperemesis gravidarum, ultrasound reveals biliary sludge and hydration concomitantly ameliorates the symptoms, jaundice and the biliary sludge".[32]

LEPTOSPIROSIS

It is an infectious disease caused by spirochete leptospira icterohaemorhagiae. Rat is the natural host. Infected urine contains spirochetes which penetrates the skin or mucosa of humans. Initial phase begins with fever,headache and petechial rashes. Hepatitis, Acute tubular necrosis, meningitis complicates the second phase. The spirochaetes may cross the placenta and cause abortions in first and second trimester and also intra uterine death.[33]

MATERIALS AND METHODS

STUDY PLACE:

Institute of Obstetrics and Gynaecology.

STUDY GROUP:

All cases of pregnancy with Jaundice in all trimesters admitted in Institute of Obstetrics and Gynaecology during the period 2011 – 2012.

STUDY DURATION:

. One year 2011-2012.

TYPE OF STUDY:

A Prospective, observational study.

INCLUSION CRITERIA:

All Antenatal mothers with Jaundice in any trimester of pregnancy.

EXCLUSION CRITERIA:

- Associated comorbid condition like renal problem, Heart disease.
- Known case of HbsAg positive patient not with Jaundice

This prospective study of maternal and fetal outcome included 51 pregnant women with Jaundice admitted in Institute of Obstetrics and Gynaecology during the period 2011 – 2012.

Elaborate history regarding Age, socio-economic status, obstetric history was obtained. Patients were enquired in detail about complaints and like nausea, vomiting, pruritus, anorexia, yellow coloured urine, pale stools, edema legs, bleeding tendency, joint pain and their duration.

Past history of jaundice especially in previous pregnancy, history of blood transfusion, history of STI and history of jaundice in family members were noted. Much importance was given in taking note of the source of drinking water.

Though general examination was done in all patients. Anaemia, jaundice, edema, bleeding gums, hepatic tremor were looked for Temperature, PR, B.P, CVS and RS findings were recorded. Abdominal examination was done to make out any liver and spleen enlargement and free fluid.

Obstetric examination was done to note the size of uterus, lie, presentation and attitude of fetus, fetal heart rate, liquor volume and rough estimation of fetal weight. Patients who were either in labour or seriously ill were admitted in labour ward for intensive care. Patients with either good general condition or not in labour were admitted in antenatal ward for further evaluation. Provisional diagnosis was arrived.

Liver function tests like S.Bilrubin total, direct and indirect, total proteins, albumin and globulin, SGOT, SGPT, S.Alkaline phospatase, clotting time, , bleeding time and USG were done. Complete hemogram and reticulocyte count were done. Coagulation profile was done for all and values were noted.

Viral markers study including HBs Ag, Anti HAV IgM, Anti HCV Ab, Anti HEV IgM by enzyme immuno assay (ELISA) technique was done. VDRL and HIV examination was done in all patients. Medical gastroenterologist opinion was obtained in nearly all cases.

Dark field microscope examination was done for leptospirosis. Blood samples were also sent for MSAT. Antibiotics were started as soon as dark field microscope results were obtained.

Labour was closely monitored with partogram. Mode of delivery was recorded. Jaundice per se was not an indication for caesarean section. Vaginal delivery with close monitoring was preferred and caesarean section was done only for obstetric indication. Blood grouping and typing was done. After cross matching fresh blood and FFP was kept ready as alternation in coagulation profile was expected in jaundice complicating pregnancy.

Soon after delivery all babies were assessed by paediatrician. Alive or dead, sex of the body, gestational age at birth, weight, Apgar score and presence or absence of any congenital anomalies were looked for and noted.

As per paediatrician opinion sick babies were admitted in preterm ward for intensive care. Babies were followed by and cause of death was noted.

OBSERVATION

A prospective study of all the antenatal patients admitted with jaundice in pregnancy at the Institute of Obstetrics and Gynaecology Chennai during 2011-2012 was undertaken.

Total number of antenatal admissons during this period was 17,890. Total number of patients with jaundice was 51 and they are the present study group.

1. INCIDENCE OF JAUNDICE COMPLICATING PREGNANCY

The incidence of jaundice complicating pregnancy during this period in our Hospital is 0.29%.

TABLE - 1

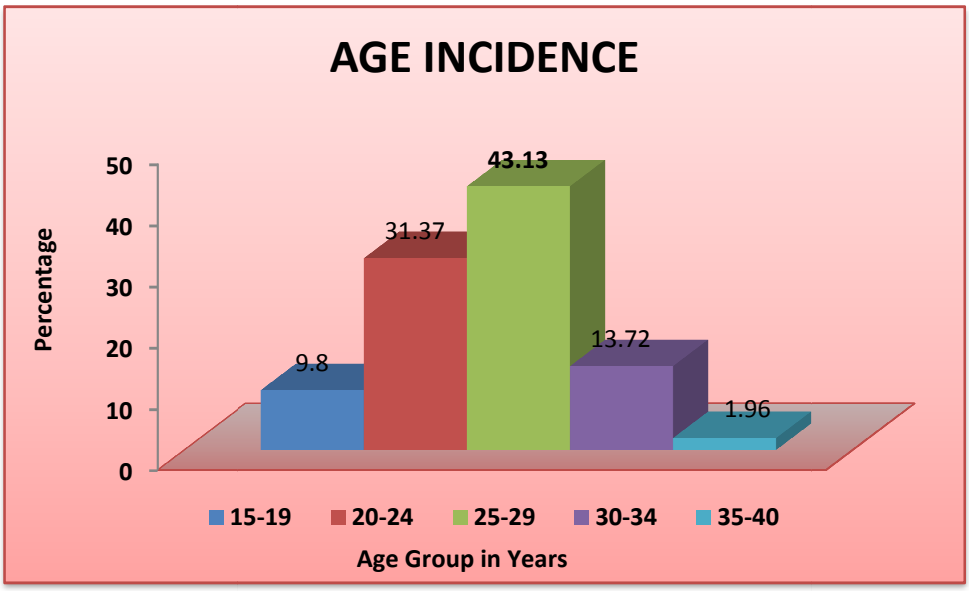
Year	Total antenatal admissions	No of Jaundiced pregnant women	Percentage	Incidence per 1000 population per year
2011-12	17890	51	0.28	2.85

AGE INCIDENCE

TABLE -2

S.No	Age group in years	No of Cases	Percentage
1	15-19	5	9.8
2	20-24	16	31.37
3	25-29	22	43.13
4	30-34	7	13.72
5	35-40	1	1.92
	Total	51	100

The patients in the study group were in the age range from 18 years to 36 years. Nearly 74% of the jaundiced patients were between 20 and 29 years.

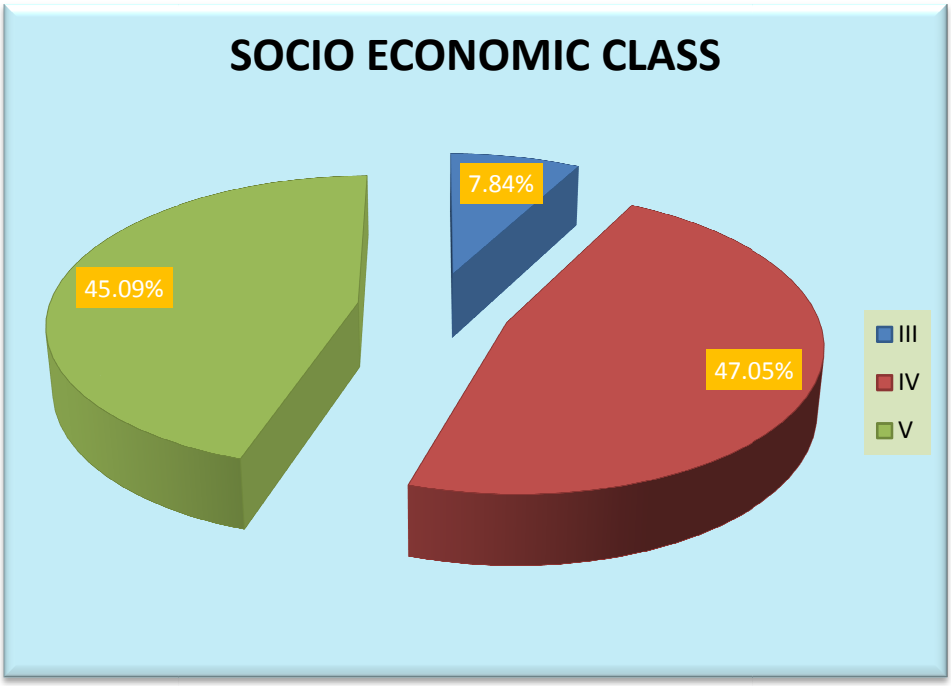


DISTRIBUTION AS PER SOCIO-ECONOMIC CLASS

TABLE – 3

S.E Class	Number of cases	Percentage
III	4	7.84
IV	24	47.05
V	23	45.09

The incidence of Jaundice is more common in low socio-economic groups. About 92.1 of cases belonged to class IV and V.

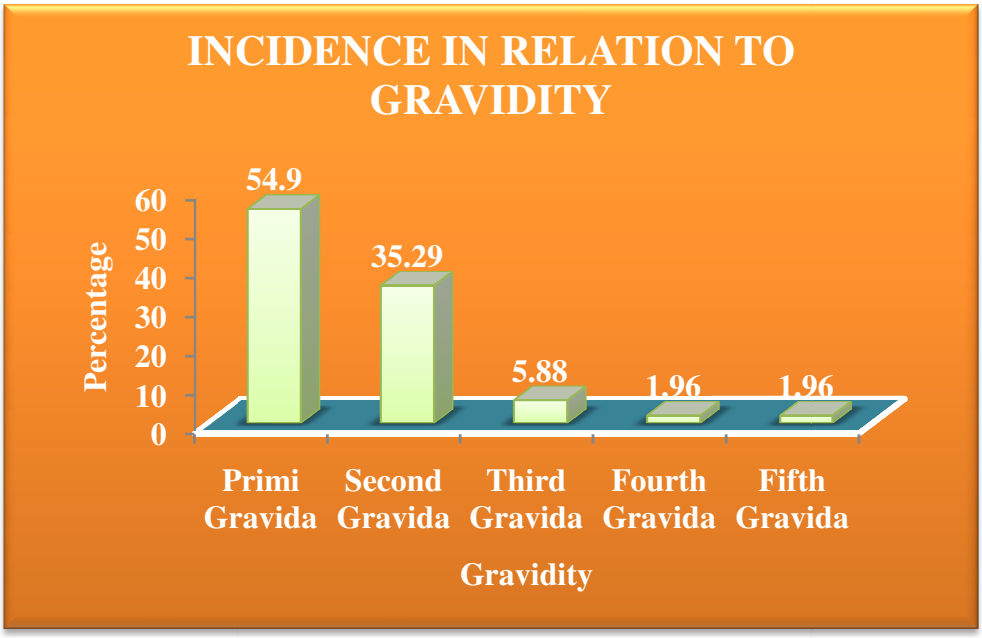


INCIDENCE IN RELATION TO GRAVIDITY

TABLE -4

S.No.	Gravidity	No.of Cases	Percentage
1	Primigravida	28	54.9
2	Second gravida	18	35.29
3	Third gravida	3	5.88
4	Fourth gravida	1	1.96
5	Fifth gravida	1	1.96

Maximum number of cases were primigravida 54.9%,second gravida were 35.29 %.

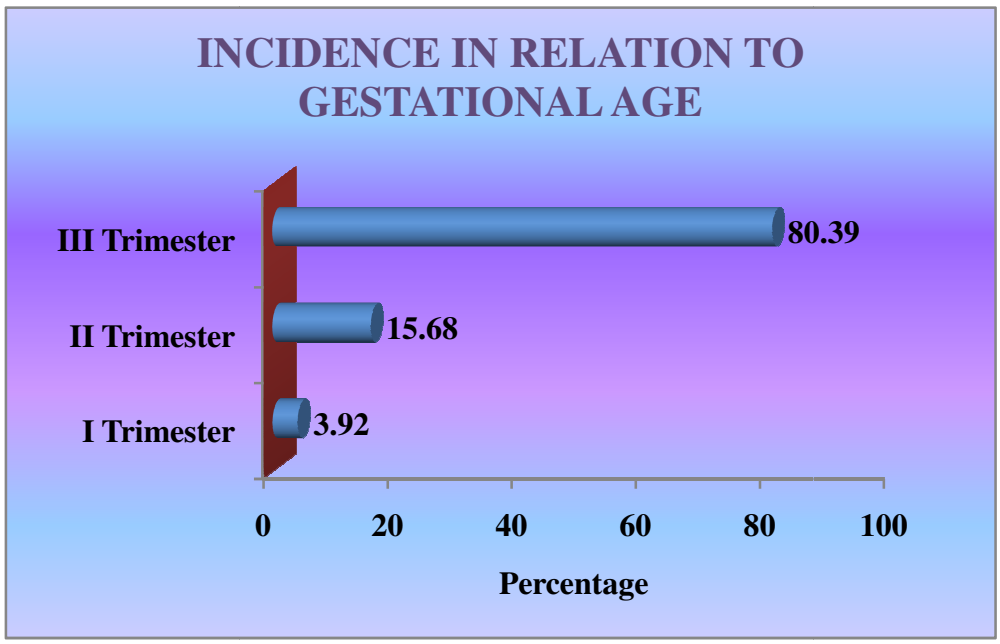


INCIDENCE IN RELATION TO GESTATIONAL AGE

TABLE -5

S.No	Period of Gestation	No.of Cases	Percentage
1	I Trimester	2	3.92
2	II Trimester	8	15.68
3	III Trimester	41	80.39

Out of 51 cases, 41 cases (80.39%) presented with Jaundice during III trimester.

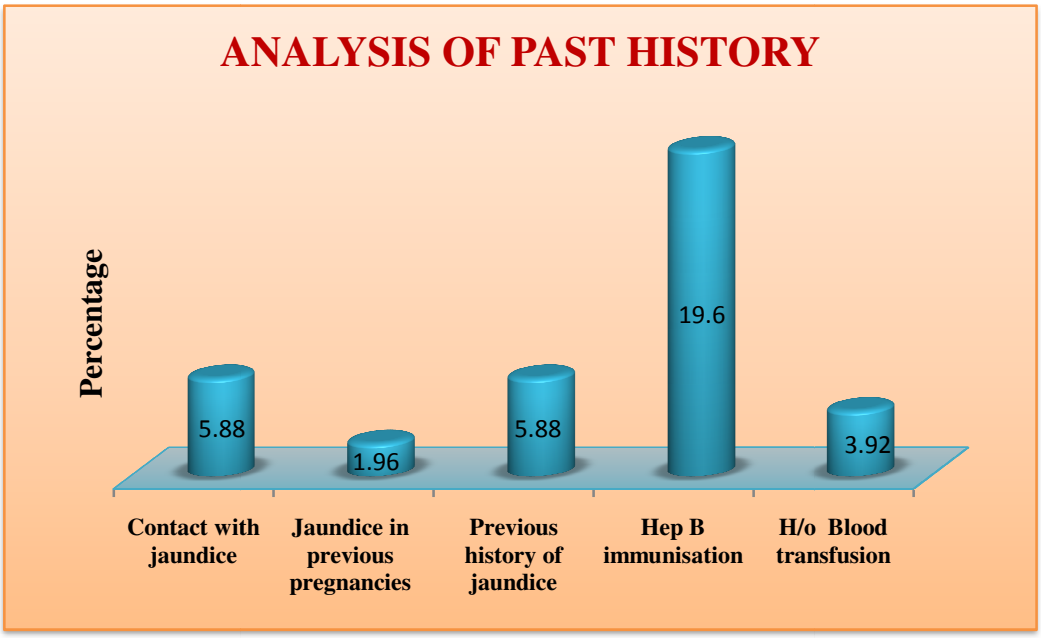


ANALYSIS OF PAST MEDICAL HISTORY

TABLE-6

S.No.	Past History	No.of Cases	Percentage
1	Contact with jaundice	3	5.88
2	Jaundice in previous pregnancies	1	1.96
3	Previous history of jaundice	3	5.88
4	Hep B immunization	10	90.6
5	H/o Blood transfusion	2	3.92

3 Patients had history of contact with jaundice. 2 patients had history of blood transfusion among which one was HBsAg positive.10 had Hepatitis B immunization.

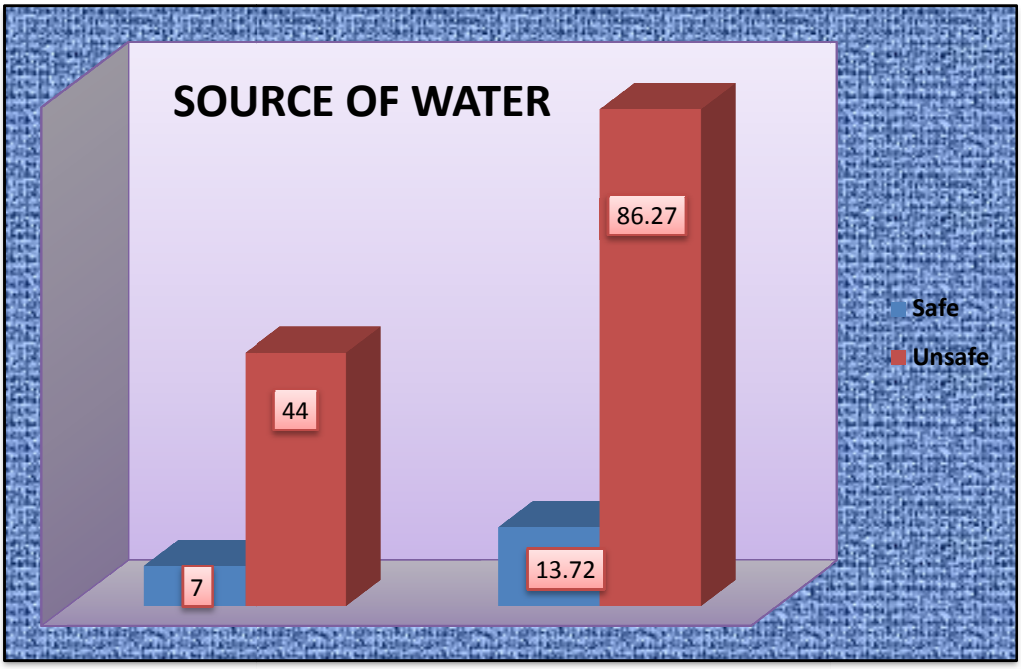


SOURCE OF DRINKING WATER

TABLE – 7

Water	Number of cases	Percentage
Safe	7	13.72
Unsafe	44	86.27

5% of patients were utilising safe water for drinking purpose and 95% patients were ignorant about safe water.

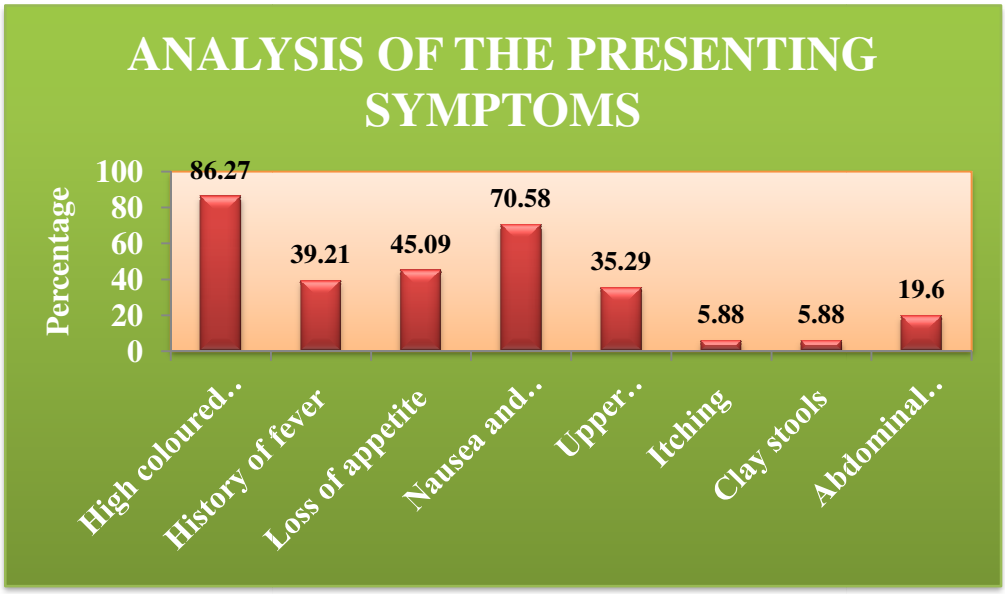


ANALYSIS OF THE PRESENTING SYMPTOMS

TABLE -8

S.No	Symptoms	No.of Cases	Percentage
1	High coloured Urine	44	86.27
2	History of fever	20	39.21
3	Loss of appetite	23	45.09
4	Nausea and vomiting	36	70.58
5	Upper abdominal pain	18	35.29
6	Itching	3	5.88
7	Clay stools	3	5.88
8	Abdominal distension	7	19.6

On analysing the presenting symptoms 86.27% had high color urine. Nausea and vomiting were present in 70.6%.Other predominant symptoms were fever, loss of appetite and upper abdominal pain. The number of cases with percentage of various symptoms are shown in Table-8.

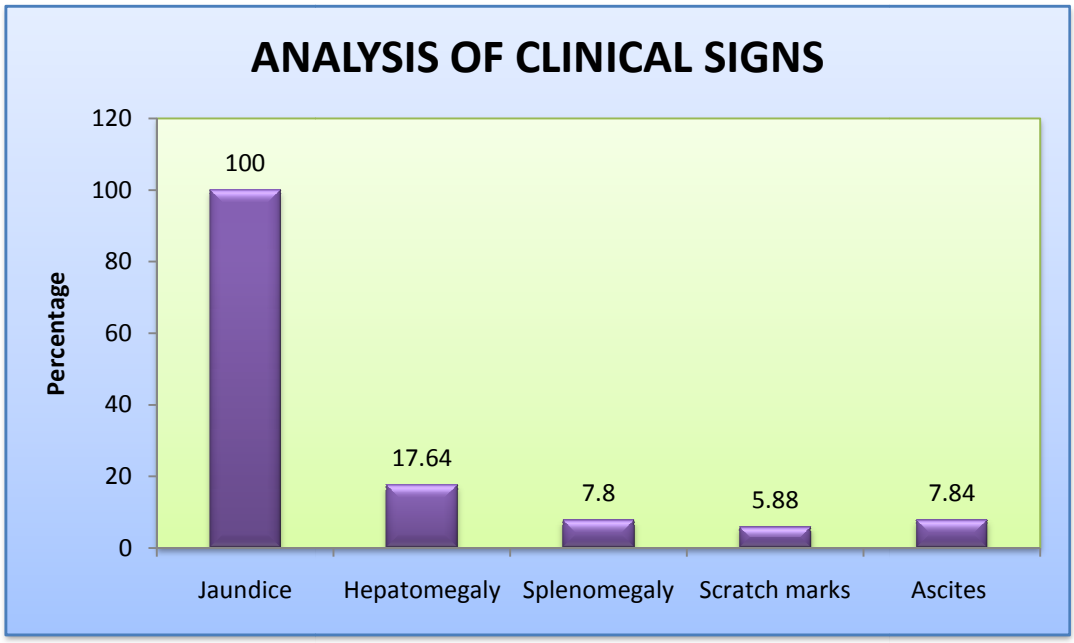


ANALYSIS OF CLINICAL SIGNS

TABLE-9

S.No	Clinical Signs	No.of Cases	Percentage
1	Jaundice	51	100
2	Hepatomegaly	9	17.64
3	Splenomegaly	4	7.8
4	Scratch marks	3	5.88
5	Ascites	4	7.84

Jaundice was present in all the cases.Other signs were Hepatomegaly, Splenomegaly, Scratch marks and Ascites.

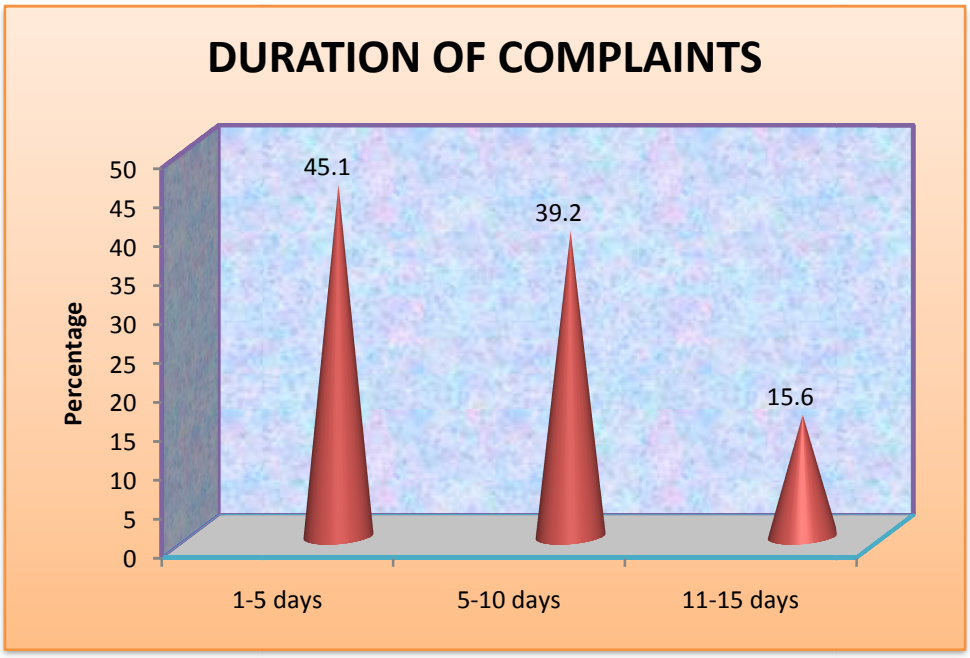


DURATION OF COMPLAINTS

TABLE- 10

Duration of Complaints	Number of cases	Percentage
1-5 days	23	45.1
5-10 days	20	39.2
11-15 days	8	15.6

45.1 % of patients had the complaints for 1-5 days.

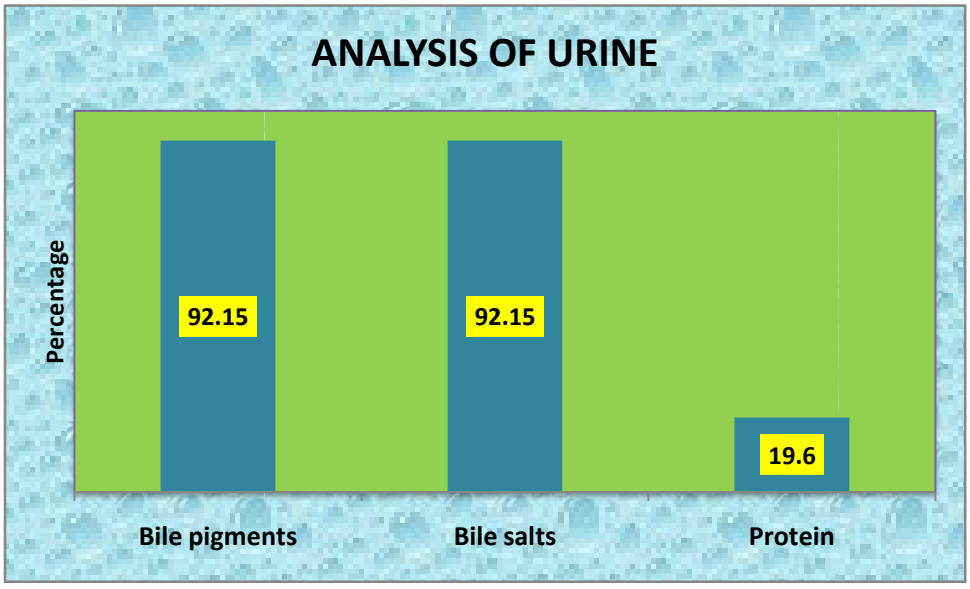


RESULTS OF URINE ANALYSIS

TABLE-11

Tests	Present	Percentage
Bile pigments	47	92.15
Bile salts	47	92.15
Protein	7	19.6

92.15% of patients showed positive for Bile pigments and Bile salts in the urine. 19.6% patients were positive for Protein.

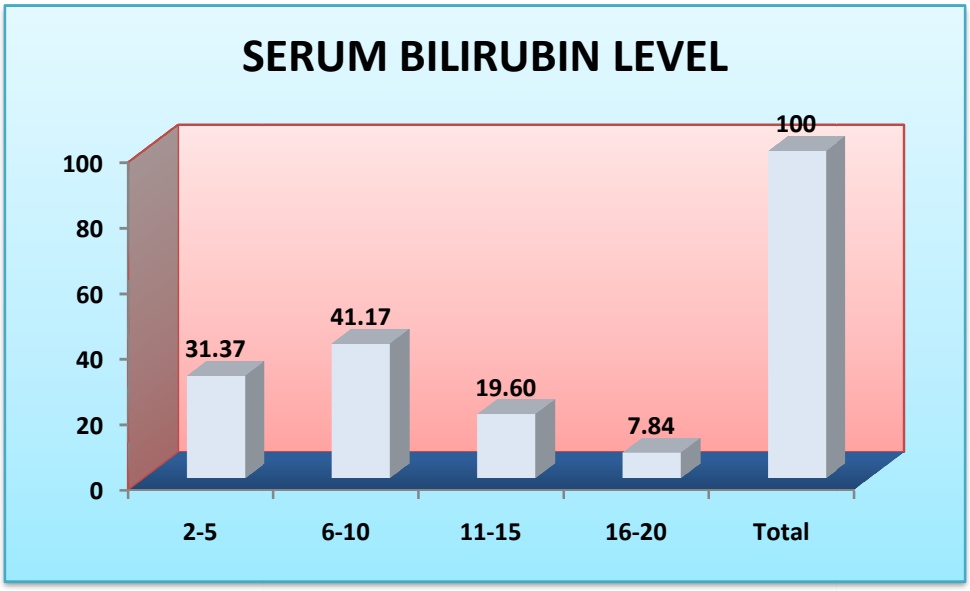


SERUM BILIRUBIN LEVEL

TABLE -12

S.No	Serum Bilirubin (mg%)	No.of Cases	Percentage
1	2-5	16	31.37
2	6-10	21	41.17
3	11-15	10	19.60
4	16-20	4	7.84

The level of S.Bilirubin varied widely between 2.8 to 18.4 mg / dl. 7.84% of patients had high S.Bilirubin more than 16 mg / dl.

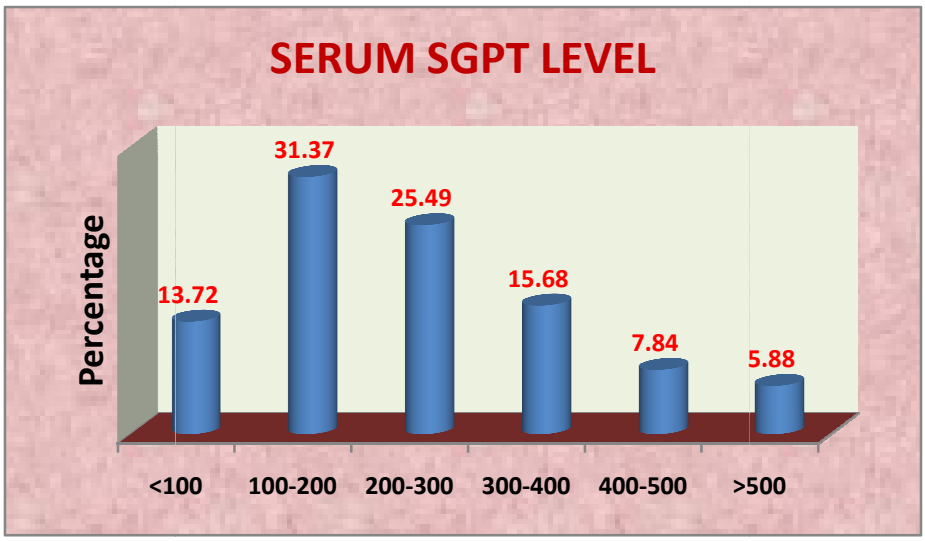


SERUM TRANSAMINASE LEVEL

TABLE-13

S.No	SGPT	No.of Cases	Percentage
1	<100	7	13.72
2	100-200	16	31.37
3	200-300	13	25.49
4	300-400	8	15.68
5	400-500	4	7.84
6	>500	3	5.88

The serum transaminase level was below 100 IU/L in 13.72% of patients. About 5.88% patients had level more than 500 IU/L.



S.ALKALINE PHOSPHATASE LEVEL

TABLE-14

Alkaline Phosphatase U/l	No.of Cases	%
Upto 200	19	37.25
200-400	21	41.17
400-600	7	13.72
600-800	2	3.92
>800	2	3.92

S.Alkaline phosphatase was more than 400 U/L in 21.5% .

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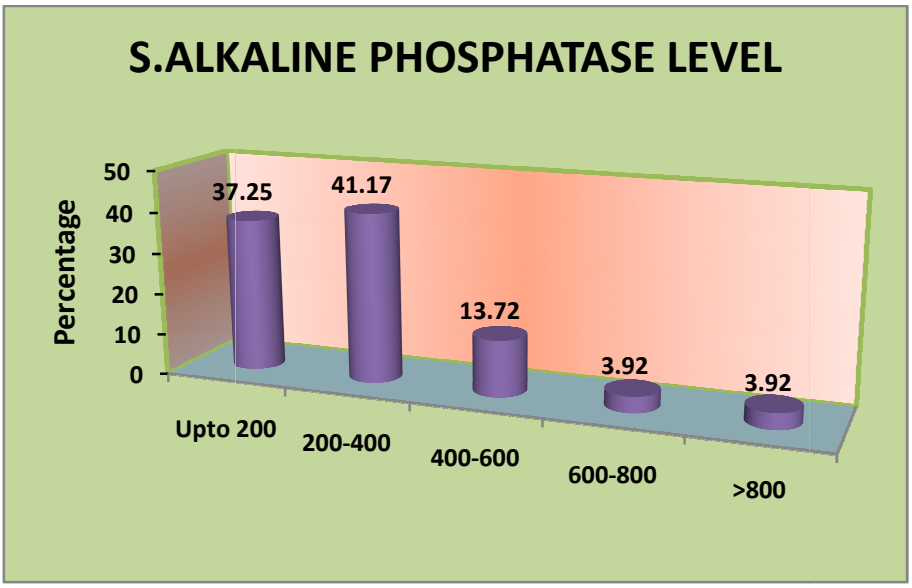
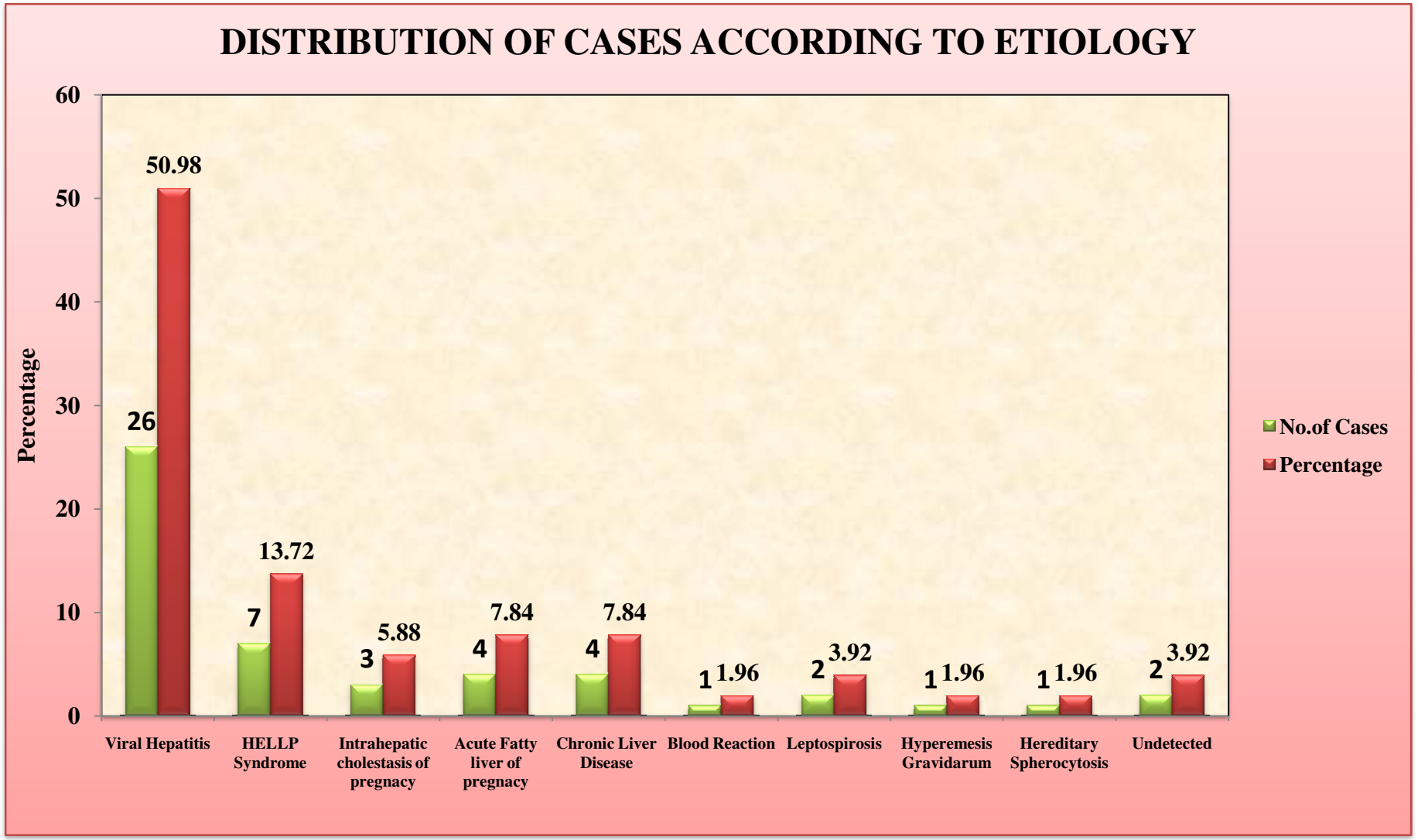


DISTRIBUTION OF CASES ACCORDING TO ETIOLOGY

TABLE – 15

S.No	Diagnosis	No.of Cases	Percentage	Incidence per 1000 Population
1	Viral Hepatitis	26	50.98	1.4
2	HELLP Syndrome	7	13.72	0.3
3	Intrahepatic cholestasis of pregnacy	3	5.88	0.16
4	Acute Fatty liver of pregnacy	4	7.84	0.22
5	Chronic Liver Disease and Portal Hypertension	4	7.84	0.22
6	Blood Reaction	1	1.96	0.05
7	Leptospirosis	2	3.92	0.11
8	Hyperemesis Gravidarum	1	1.96	0.05
9	Hemolytic jaundice (Hereditary Spherocytosis)	1	1.96	0.05
10	Undetected	2	3.92	0.11

Viral hepatitis was the commonest etiology in 50.98%.Of this, Hepatitis E detected in 14 cases, Hepatitis B detected in 10 cases. HELLP Syndrome was the next common etiology in 30.72%.Acute Fatty liver of pregnancy and Chronic Liver Disease with Portal Hypertension were the cause in 7.84%. Hemolytic jaundice due to Hereditary Spherocytosis was seen in one patient. The cause was Undetected in 2 cases.

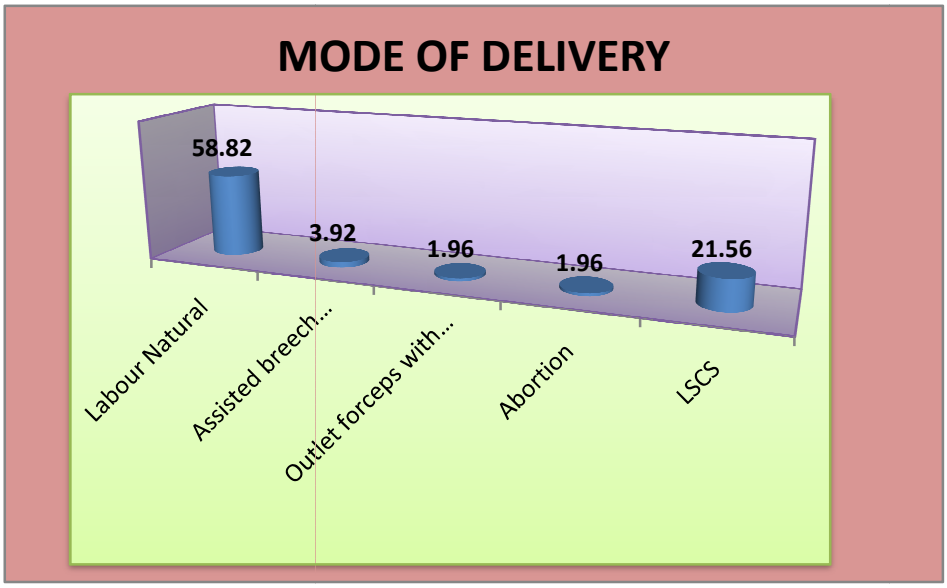

DISTRIBUTION OF CASES ACCORDING TO ETIOLOGY
Percentage
60
50
40
30
20
10
0
50.98
26
13.72
7
5.88
3
7.84
4
7.84
4
1.96
1
3.92
2
1.96
1
1.96
1
3.92
2
Viral Hepatitis
HELLP Syndrome
Intrahepatic cholestasis of pregnacy
Acute Fatty liver of pregnacy
Chronic Liver Disease
Blood Reaction
Leptospirosis
Hyperemesis Gravidarum
Hereditary Spherocytosis
Undetected
No.of Cases
Percentage

MODE OF DELIVERY

TABLE -16

Mode	Number of cases	Percentage
Labour Natural	30	58.82
Assisted breech delivery	2	3.92
Outlet forceps with episiotomy	1	1.96
Abortion	1	1.96
LSCS	11	21.56

Out of 51 patients, 45 delivered. 4 patients who were in II trimester and 1 in I trimester got discharged after treatment. 1 patients died antenatally. 70% patients delivered vaginally. 21.56% patients had LSCS.

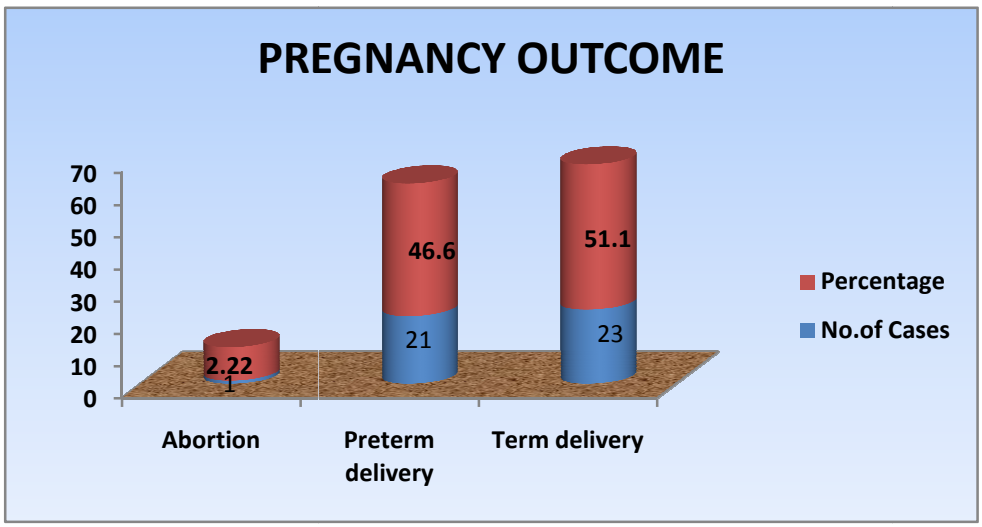


PREGNANCY OUTCOME

TABLE -17

S.No	Pregnancy outcome	No.of Cases	Percentage
1	Abortion	1	2.22
2	Preterm delivery	21	46.66
3	Term delivery	23	51.11
	Total	45	100

Out of 45 patients 23 had Term delivery, 21 patients had Preterm delivery ,one had abortion.



MATERNAL OUTCOME (2011-2012)

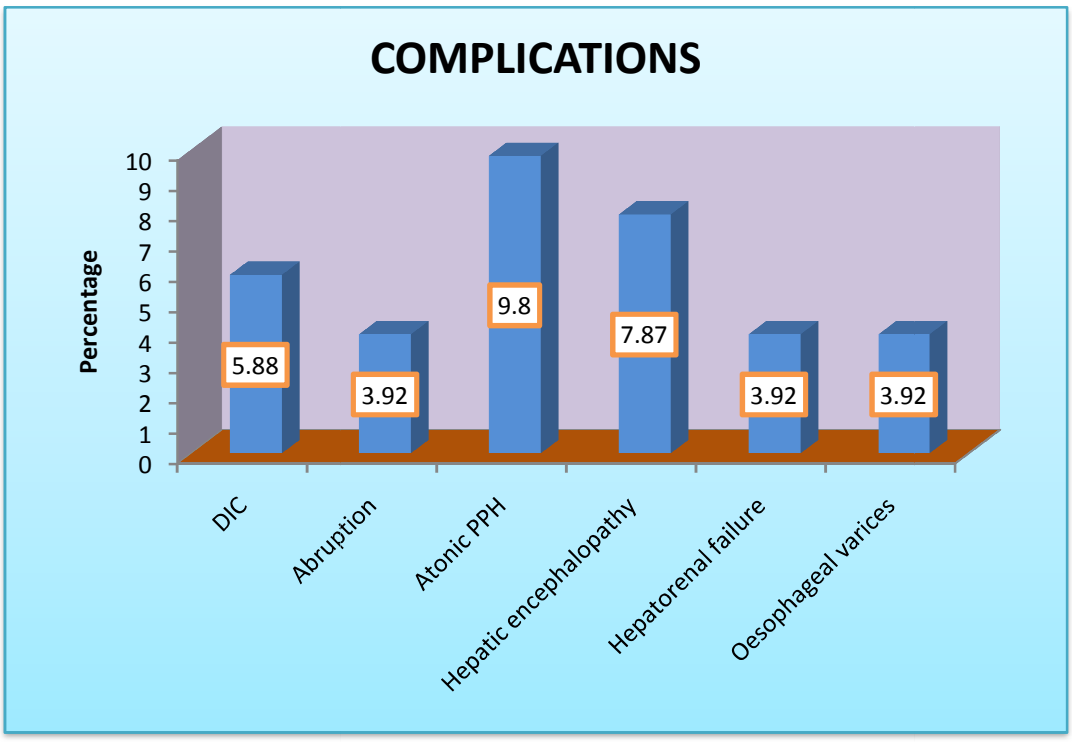
Table - 18

1	**Total number of antenatal admissions**	**17890**
2	Total number of maternal mortality	32
3	Incidence of maternal mortality	1.78/1000 population
4	Total number of jaundiced cases	51
5	Total number of mortality due to jaundice	4
6	% of mortality in jaundice	7.8%
7	% of mortality due to jaundice in relation to total maternal mortality	12.50%

TYPE OF COMLICATIONS
TABLE -19

Complications	Number of cases	Percentage
DIVC	3	5.88
Abruption	2	3.92
Atonic PPH	5	9.8
Hepatic encephalopathy	4	7.87
Hepatorenal failure	2	3.92
Oesophageal varices	2	3.92
Total	18	35

In four patients Hepatic encephalopathy was seen. Atonic PPH was seen in 5 patients. DIVC was seen in 3 patients.

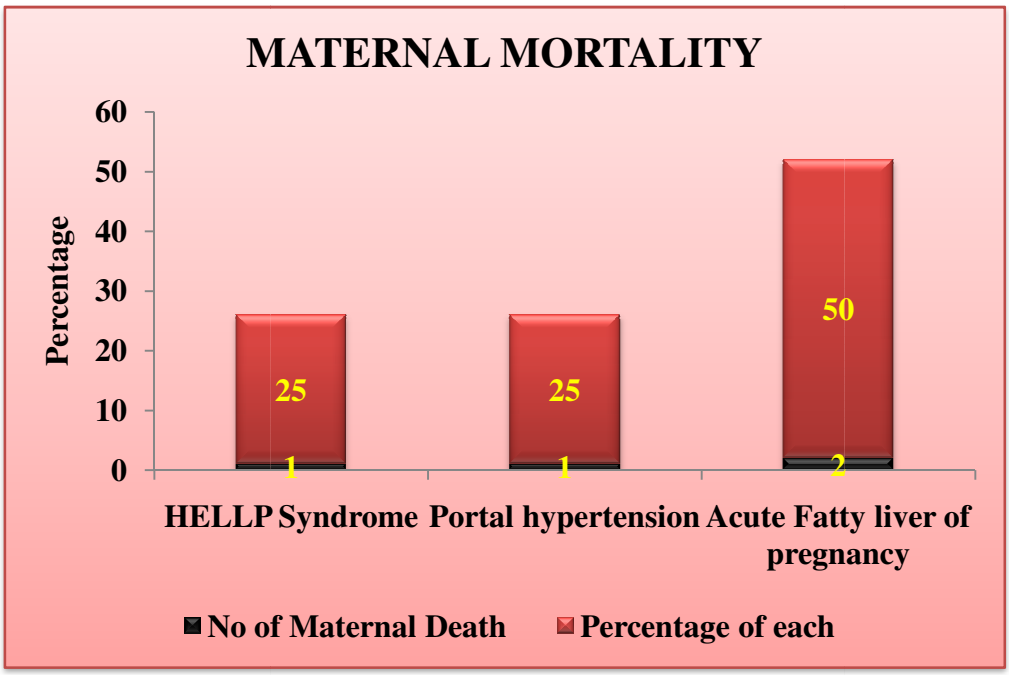


CAUSES OF MATERNAL MORTALITY

TABLE - 20

S.No	Diagnosis	No.of cases	Maternal Mortality	Percentage
1	HELLP Syndrome	7	1	25
2	Portal hypertension	4	1	25
3	Acute Fatty liver of pregnancy	4	2	50

Among 4 deaths two were due to Acute fatty liver of Pregnancy, one died of HELLP and one due to rupture of Esophageal varices.



RELATION OF SERUM BILIRUBIN TO MATERNAL MORTALITY

TABLE-21

S.No	Serum Bilirubin level (mg%)	No of Patients	Maternal Mortality	Percentage of Maternal Mortality
1	2-5	16	1	25
2	6-10	21	1	25
3	11-15	10	2	50
	Total	51	4	100

Among 4 cases two had S.bilirubin more than 10 gm/dl.

RELATION OF SERUM TRANSAMINASE LEVEL TO MATERNAL MORTALITY

TABLE – 22

S.No	SGPT	No.of Cases	Maternal Mortality	Percentage of Maternal Mortality
1	<100	7	0	0
2	100-200	16	1	25
3	200-300	13	1	25
4	300-400	8	1	25
5	400-500	4	1	25
6	>500	3	0	0

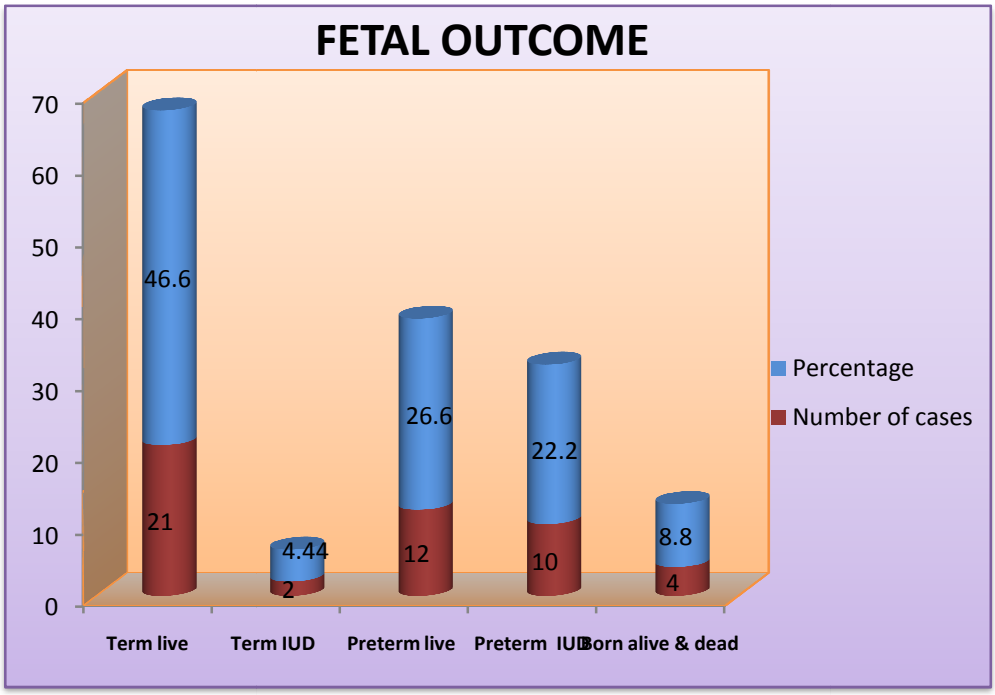
Serum transaminase level had no relation to maternal mortality.

FETAL OUTCOME

TABLE – 24

Outcome	Number of cases	Percentage
Term live babies	21	46.6
Term IUD babies	2	4.44
Preterm live babies	12	26.6
Preterm still Birth / IUD	10	22.2
Born alive & dead (all preterm)	4	8.8
Perinatal mortality	16	35.5

Perinatal mortality was 35.5% of these 80% was due to prematurity. There were 37 live birth .Of these 16 were preterm. 21 were Term babies.4 preterm babies born alive,died during neonatal period.

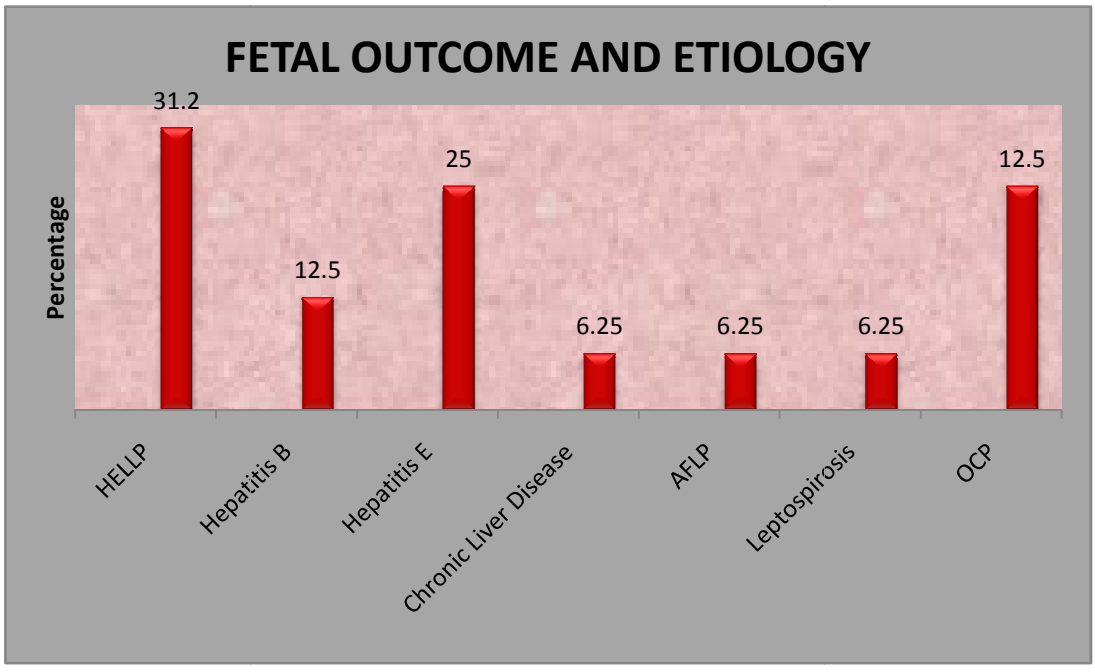


CORRELATION OF PERINATAL MORTALITY WITH ETIOLOGY.

TABLE - 25

Etiology	No of perinatal deaths	%
HELLP	5	31.25
Hepatitis B	2	12.5
Hepatitis E	4	25
Chronic Liver Disease	1	6.25
AFLP	1	6.25
Leptospirosis	1	6.25
OCP	2	12.5
Total	16	100

Poor fetal outcome was seen with HELLP syndrome 31.25%, Hepatitis E 25%, Hepatitis B 12.5%, and intrahepatic cholestasis 12.5%.



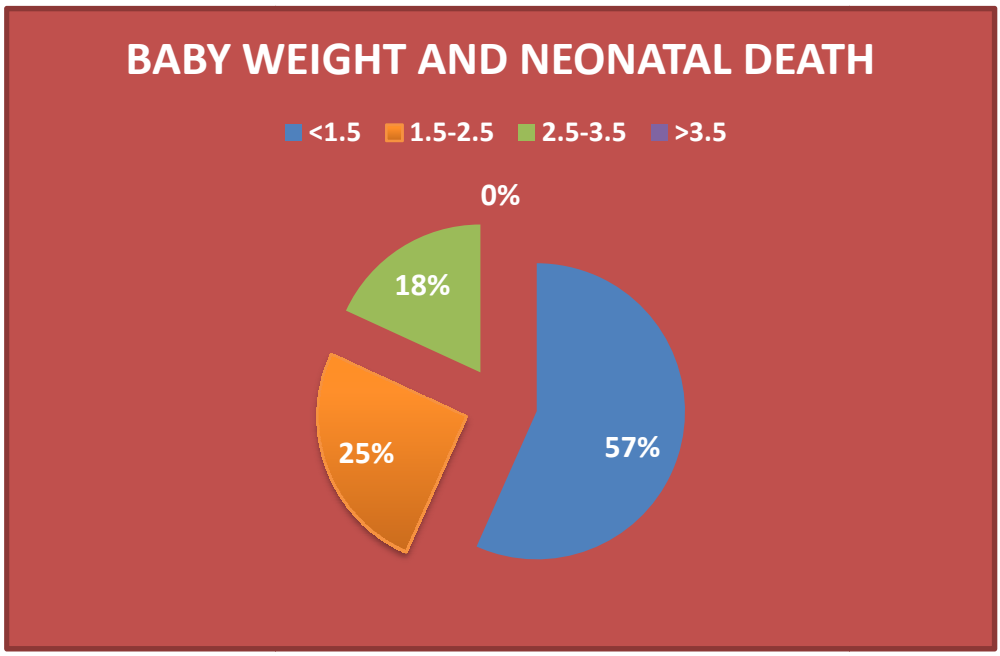
INFLUENCE OF BABY WEIGHT ON FETAL OUTCOME

TABLE -26

S.No	Baby weight (kg)	No of babies	Neonatal death	Percentage of Neonatal death
1	<1.5	11	9	56.25
2	1.5-2.5	13	4	25
3	2.5-3.5	20	3	18
4	>3.5	1	0	0

24 babies were below 2.5 kg and among them, there was 80% mortality.

Most of them were preterm.



DISCUSSION

INCIDENCE: The incidence of jaundice in pregnant women at institute of obstetrics and Gynaecology (IOG) Chennai during 2011-2012 (1 year) was 0.28%. i.e. 2.85 per 1000 population. In India the incidence is between 0.1 to 0.4%.

The incidence quoted in studies from various places:

Sarkar et at (Calicut) 1992 0.23%

Reddi Rani et at (Pondicherry) 1993 0.11%

DevinderKaur et at (Delhi) 2001 0.09%

Institute of obstetrics and Gynaecology 2002 0.14%

The reason for varied incidence may be due to many patients with mild icterus not seeking medical attention.

AGE: In our study, 31.3% patients were in the age group of 20-24 years. 43.13% patients were in the age group 25-29 years which showed the increase in the mean age of marriage nowadays.

SOCIO ECONOMIC STATUS: 92% of our study group belonged to lower socio economic class and 86% were consuming unsafe water. Hepatitis E and Hepatitis A are more prevalent in lower socio economic

class due to unsafe drinking water, lack of sanitation and poor personal hygiene.

Nargis Begum et al 2009 studied about the seroprevalence (IgG Anti HEV) of subclinical HEV infection in pregnant women and reported that exposure to Hepatitis E was more in lower socio economic class.[34]

GRAVIDITY AND GESTATIONAL AGE

Primigravida and second gravida were common (90%) in our study group.Among them 55% were Primigravide.

80% of our patients were in III trimester. Harshad et al 2008, Shukla et al 2011 and other studies have stated that maximum incidence of jaundice was in III trimester and morbidity and mortality were also higher during III trimester.

PAST HISTORY:

In this study 3 patients had contact with Jaundice. Two had history of blood transfusion and among them 1 had Hepatitis B infection. Among the 3 patients diagnosed as intra hepatic cholestasis of pregnancy, one had history of jaundice in her mother during her antenatal period and one patient had twin pregnancy.

SYMPTOMS AND SIGNS

All patients were icteric (100%). Nausea and vomiting in 70.5% cases, loss of appetite in 45% cases, Fever in 39% cases, upper abdominal pain in 35% cases were the other predominant symptoms. Hepatomegaly was found in 9 patients. Splenomegaly was found in 4 patients who had chronic liver disease and 4 patients had ascites.

ETIOLOGY

Viral Hepatitis was the etiology in 51% of cases, HELLP syndrome in 13.72% patients, Acute fatty liver of pregnancy in 7.8% patients chronic liver disease in 5.9% patients intra hepatic cholestasis in 5.9% patients. Other uncommon causes were Leptospirosis in 3.92%, Blood reaction in 1.96%, Hyperemesis in 1.96%, Hemolytic Jaundice in 1.96% The cause for Jaundice was undetected in 2 cases.

VIRAL HEPATITIS: Viral Hepatitis was the cause in 51% cases comparable to the study by Shukla et al 2011 who reported 57% and Harshad et al 2008 reported 47% cases of viral hepatitis.[35,36]

Prevalance of Viral Hepatitis in Pregnant Women.

Hepatitis A -	Patra et al 2005	Delhi 0.5%
	Beniwal et al 2005	Delhi 5.2%
Hepatits B. -	Harshad et al 2008	Bangalore 16%
	Rathi et al 2007	Mumbai 5%
	Shukla et al 2011	Delhi 37%
Hepatits E. -	Harshad et al 2008	Bangalore 31%
	Rathi et al 2007	Mumbai 14%
	Shukla et al 2011	Delhi 18%
Hepatits C. -	Shukla et al 2011	Delhi 4%
	Beniwal et at 2005	Delhi 0%

In this present study, Hepatitis E was diagnosed in 23% cases, Hepatitis B in 21% cases and Hepatitis A in 5.8% cases.

HELLP SYNDROME: 13.72% of cases had HELLP Syndrome in our study. Rathi.U et al 2007 reported 52.3% of cases with liver dysfunction due to preeclampsia and HELLP.[37]

CHRONIC LIVER DISEASE : 4 cases had chronic liver disease. Among them, 3 had non-cirrhotic portal hypertension (NCPH). Agarwal et al 2001 studied 50 pregnant patients with NCPH and reported that in 56 % patients. NCPH was detected first during pregnancy. In India Portal hypertension is commonly due to Non cirrhotic portal fibrosis and extra hepatic portal vein obstruction (EHPVO). But in western countries Portal hypertension is mostly due to cirrhosis.[38]

ACUTE FATTY LIVER OF PREGNANCY: AFLP was diagnosed in 4 cases with the clinical features and biochemical parameters. All of them had more than 6 features of Swansea criteria for AFLP.

INTRA HEPATIC CHOLESTASIS: Intra hepatic cholestasis of pregnancy was diagnosed in 3 patients, one had history of jaundice in her mother during her antenatal period and one patient had twin pregnancy.

HEREDITARY SPHEROCYTOSIS: We had one case of hemolytic jaundice due to hereditary spherocytosis. Pajor et al 1993 studied 19 pregnancies with hereditary spherocytosis, concluded that pregnancy

precipitated hemolytic anaemia and maternal and fetal outcome was favourable after splenectomy.[31]

OTHERS: Leptospirosis was diagnosed in 2 cases by MSAT. Shalini et al (2009) reported a case of leptospirosis with Jaundice, coagulopathy and intra uterine death.[33]

One was due to Hyperemesis gravidarum. Matsubara's et al reported that Jaundice in Hyperemesis is due to biliary sludge and it is relieved by hydration.[32,41]

BIOCHEMICAL PARAMETERS

In our study, SGPT and SGOT levels more than 500 IU/ml were associated with viral hepatitis. Harshad et al 2008 also reported that marked elevation of bilirubin and transaminases (10 fold) occured in viral hepatitis whereas patients with pregnancy associated liver disease like HELLP, Intrahepatic cholestasis and Hyperemesis had only 2-3 fold elevation.[36]

MANAGEMENT

Patients with Mild Jaundice were managed with supportive measures like Bed rest, Intravenous Dextrose, High carbohydrate diet, Vitamin K and Syrup Lactulose. Ursodeoxycholic acid tablets 500 mg BD was given

to patients with pruritus. Severe cases required intensive care management. 22 patients were transfused blood and 27 patients were transfused fresh frozen plasma. Obstetric interventions were done for HELLP and AFLP. All patients were monitored with serial Liver function tests and coagulation profile until recovery.

PREGNANCY OUTCOME: Among the 57 patients 5 patients were recovered and discharged. One patient died antenatally. 23patients had term delivery, 21 had preterm delivery and 1 patient had therapeutic abortion due to hemolytic crisis in hereditary spherocytosis.

MATERNAL OUTCOME:

In the present study 7.8% patients died, 35 % patients developed complications and 58% had uneventful recovery.

Complications: 9.8% patients had atonic PPH. 5.8% had DIVC, 7.8% had Hepatic encephalopathy. Abruption, Hepatorenal failure, Esophageal varies was seen in 3.9 % each.

The patients with atonic PPH, DIVC, and Abruption were treated with blood, fresh frozen plasma and platelets. 2 patients with renal failure recovered with multiple sittings of dialysis.

Jain.S et al 2000 reported 52 patients with fulminant hepatic failure and concluded that renal dysfunction was the indicator of poor prognosis in patients with fulminant hepatic failure.[39]

CAUSES OF MATERNAL MORTALITY

Among 4 deaths two were due to Acute fatty liver of Pregnancy, one died of HELLP and one due to rupture of Esophageal varices.

AFLP: The two patients were primigravida and in III trimester. Both had vomiting, abdominal pain, High bilirubin, High transaminases, Coagulopathy (raised prothrombin time) and Encephalopathy.

Apart from the above findings one patient had leucocytosis, Hypoglycemia, bright liver on USG and the other had ascites and renal impairment. One had intrauterine death and other had a live baby , and both delivered by normal vaginal delivery. Their condition deteriorated soon after delivery, developed Grade III encephalopathy was on ventilatory support but could not be revived.

Rathi .U et al 2007 reported 3 cases of AFLP and among them 2 cases died of DIVC and multiorgan failure.[37]

Third patient died of HELLP syndrome, had severe hypertension, proteinuria, ascites delivered a dead born baby, died of DIVC and

Hepatorenal failure.Rathi.U et al 2007 reported 25% mortality due to Preeclampsia associated liver dysfunction.

The fourth patient was a case of Non-cirrhotic portal hypertension with grade III Esophageal varices died due to massive hematemesis during second trimester. She was an unbooked case.

Study by Peitsidou et al 2007 showed that risk of variceal bleeding increased to 62-78% if endoscopy revealed esophageal varies and should be treated by sclerotherapy or variceal ligation. Agarwal et al (1999) reported that esophageal varices was the most feared complication of portal hypertension. West brook et al (2011) reported one death in pregnancy due to variceal bleeding.[40]

Mortality due to viral hepatitis was not seen in the present study though many patients of hepatitis E had severe morbidity. Study by **Jayanthi&Udayakumar et al 2008, Chennai**[42]observed that mortality rate of Hepatitis E infection in southern India was very low 3-4% compared to high mortality 30-100% seen in studies from Northern India. Study by **Harshad et al 2008,** Bangalore reported that mortality was 41% in pregnancy associated liver disease and 7.5% in viral hepatitis and concluded due to Hepatitis E was low.

FETAL OUTCOME

In the present study among 45 live births, 33 (73.4%) were live births 12(26.6%) were intra uterine deaths. Preterm deliveries were 48.8% (26.6% live birth and 22.2% intra uterine deaths).

The higher incidence of preterm delivery supported by Veronica et al (2006) 56%, Kumar et al (2003) 66.6% and Harshad et al (2008) 32% is due to high fever, increased cytokine release, disturbed hormonal status and debilitating effects of viremia of hepatitis.

The perinatal mortality in our study was 35.5% comparable to Rathi.U et al 2007 who reported 35.4% and Kumar et al reported 26.5%.[43]

Among 16 Perinatal deaths, HELLP syndrome constituted 31.2%, Hepatitis E 25%, Hepatitis B 12.5%, and intrahepatic cholestasis 12.5%. According to Williamson et al 2011, the poor fetal outcome in intrahepatic cholestasis of pregnancy was due to the toxic bile acid level in the fetus causing fetal arrhythmia.

One intrauterine death was seen with chronic liver disease. Westbrook et al 2011 reported 26% of fetal loss with chronic liver disease.53.3% babies were below 2.5 kg in our study and among them there was 80% mortality. Shukla et al 2011 reported 30.8% low birth weight babies.

SUMMARY

1. The study was done in Institute of Obstetrics and Gynaecology, Egmore Chennai for one year(2011-2012)
2. The study was done with an aim to diagnose the cause, to assess the maternal and fetal outcome and to analyse the preventive measures.
3. Total antenatal admissions during the study period was 17890 of which 51 patients had jaundice and the incidence was 0.29%.
4. Major portion of study population belonged to the age group 20-30 years and constituted about 75%.
5. Incidence of jaundice was highest among primigravida (52%).
6. About 92% patients belonged to lower socioeconomic class and 86% were consuming unsafe water.
7. The maximum incidence of jaundice was in 3rd trimester and the complications were also high during that period.
8. Most of the patients 86% had yellowish discoloration of urine. The other predominant symptoms were nausea and vomiting, fever, loss of appetite and abdominal pain.
9. All the patients were jaundiced 100%. Splenomegaly was detected in patients of chronic liver disease (CLD) and ascites found in both HELLP syndrome and CLD patients.

10. Bile salts and bile pigments were positive in the urine of 92% patients
11. High level of S.Bilirubin and S.Transaminase levels were noticed in viral hepatitis.
12. Complication were severe in 18% patients(35%).
13. Viral hepatitis was the commonest etiology in 51% patients, the next was HELLP syndrome in 13.7%
14. 3 cases of intrahepatic cholestasis of pregnancy was diagnosed among which one had twin pregnancy and one had history of jaundice in her mother during her antenatal period.
15. Maternal mortality rate was 7.8% .Among 4 patients who died, 2 had acute fatty liver of pregnancy, one had HELLP syndrome and one had Non-Cirrhotic portal hypertension.
16. Normal vaginal delivery occurred in 58% patients and 21% patients had LSCS.
17. Blood was transfused in 22 patients, FFP in27 patients.
18. Preterm delivery was high in our study constituting 46% and the term delivery was 51% .
19. The preterm intrauterine death was 22.2% and term intrauterine death was 4.44%.
20. Among the 2 term intrauterine death one due to hepatitis B and one due to hepatitis E.

21. The neonatal mortality was 35% and among them 90% was preterm.
22. HELLP syndrome and hepatitis E were the major cause for poor fetal outcome.
23. About 55% babies weighed less than 2.5 kg and mortality was 80% among them.

CONCLUSION

Although liver dysfunction is infrequently seen in pregnancy, it can result in severe maternal and fetal compromise.

Failure to the screen for Hepatitis B can result in a newborn that will be a hepatitis carrier for life. Hence, obstetrician must remain vigilant.

Jaundice co-existent with pregnancy is a burning problem in 21st century.

By evaluating various socio-economic factor, etiological factors, maternal and fetal outcome following points arrived.

- All antenatal cases should be booked.
- All pregnant patients should be screened for Hepatitis B.
- Safe drinking water should be provided for all.
- Proper sanitation facilities and sewage disposal should be made available to all.
- Women health education to be made compulsory.
- Improved sanitary precautions should be taught during antenatal visits.
- Hazards of promiscuity to be explained.
- Health workers should be trained in diagnosing jaundice early and should refer to higher centres.

- Health education regarding all the above should be given to pregnant patients at the time of first booking.
- All cases of Jaundice complicating pregnancy should be delivered in tertiary centres where facilities for blood and blood products are available.
- Leptospirosis also to be kept in mind.
- Detection and correction of coagulation failure earlier reduces mortality.
- Babies of Hepatitis B surface Ag positive mothers should be immunised against Hepatitis B.
- Good NICU is must to manage the preterm babies.
- Awareness about jaundice and its complications should reach every obstetrician.

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INSTITUTE OF OBSTERICS AND GYNAECOLOGY

EGMORE – CHENNAI

DISSERTATION – JAUNDICE IN PREGNANCY

Serial No :

Name : Age : IP No :

Address : Occupation : Income:

Socioeconomic Status

I	II	III	IV	V

Booked	Un Booked

Religion :

Gravida :

Primi	Multi				
	1	2	3	4	>4

LMP :

EDD :

D.O.A : Time :

D.O.Delivery : Time :

D.O. Discharge: Time :

A.M.A/ Death : Time :

Gestational Age at Admission :

I tri	II tri	III tri	Labour

Obstetric Table :

G	P	L	A

Complaints:

- € Nausea, vomiting
- € Malaise, Pruritus
- € Anorexia
- € Yellow colored urine
- € Pale stool
- € Swelling of legs
- € Joint Pain
- € Bleeding tendency
- € Others

Past History :

- € H/O Jaundice in previous pregnancy
- € H/O blood transfusion
- € H/O Contact with jaundiced Pt
- € H/O Any surgery
- € H/O Hepatitis immunization

Marital History :

Personal History :

Dietary Habit :

Source of Drinking Water :

General Examination :

- € Fever
- € Anaemia, Cyanosis
- € Icterus
- € Pedal edema
- € Hepatic tremor
- € Petechia Hmge
- € Free fluid

Eyes	Tongue	Palms	Soles	Palate

Vital Data :

- € PR :
- € BP :
- € CVS :
- € RS :
- € CNS :

P/A Liver :

Spleen

Uterus : Size

Fetus

Single	Multiple

FH :

Present	Absent

Presenting Part :

Investigations :

- Urine Albumin
- Urine Sugar
- Blood Hb%
- Blood Urea
- Blood Sugar
- S.Creatinine
- S.Bilirubin T
- S.Bilirubin D
- S.Bilirubin I
- T.Proteins
- Albumin
- Globulin
- S.Uric acid
- SGOT
- SGPT
- S.Alkaline Phosphatase
- Complete Hemogram
- USG
- CT, CRT, B.T.

Viral Markers:

- € IgM anti HAV
- € HB (s) Ag
- € IgM anti HBC
- € Anti HCV Ab
- € IgM anti HEV

Diagnosis - Provisional : Final :

Management :

Supportive R_x / Antiviral drugs.

Labour :

Spont	Induced

Onset of labour
Time of Onset of labour / induction
Time of rupture of membranes
Duration of I stage
Duration of II stage

Mode of delivery :

Vaginal		Instrumental		Caesarean	
LN	*LN with epi*	*Forceps*	*Vacuum*	*Emergency*	*Elective*

Prophylactic Methergin / Oxytocin

Normal	Excessive

Amount of blood Loss

Management of PPH – Blood transfusion : surgery:

Maternal Outcome :

Morbidity - infection / PPH
Mortality -
Complete recovery - Duration from admission
Admission - Delivery interval
Delivery - Discharge / Death interval

Fetal Outcome :

1.

Alive	*Dead*	*Still Birth*	*BAD*

2. Sex

Male	Female

3.

Pre Term	Term	Postmature

4. Weight

<1.5kg	1.5-2.5kg	2.5-3.5kg	>3.5kg

5. Apgar 1’
5’

6. Any congenital anomalies / Neonatal Jaundice

7. If Born alive dead – cause of death .

PATIENT CONSENT FORM

STUDY TITLE: **A PROSPECTIVE STUDY ON MATERNAL & FETAL OUTCOME IN JAUNDICE COMPLICATING PREGNANCY** **STUDY CENTRE:**

Institute of Obstetrics and Gynaecology, Egmore, Chennai.

PARTCIPANT NAME: AGE: I.D.NO:

I confirm that I have understood the purpose of the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.

I understand that investigator, the institution, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to, undergo complete physical examination, and diagnostic tests including hematological, and ultrasonogram examinations for me.

I hereby consent to participate in this study on "**A PROSPECTIVE STUDY ON MATERNAL & FETAL OUTCOME IN JAUNDICE COMPLICATING PREGNANCY**".

Place: Signature of the Patient:

Date: Address:

Signature of the witness: Signature of Investigator:

MASTER CHART

S.NO	NAME	AGE	IP.NO	SE STATUS	SAFE WATER	OH	WOG	SYMPTOMS	DURATION DAYS	SIGNS	S.BILURUBIN			SGPT	SGOT	SAP
											TOTAL	ID	DIRECT			
1	SANDHYA	23	23253	4	US	PRIMI	35	1,3,4,5	7	1	9.1	8.2	1.2	256	225	305
2	BHUVANARATHA	26	25060	4	US	PRIMI	38	1,3,4,7	5	1,3	7.2	5	2.2	187	176	143
3	MUTHULAKSHMI	23	26485	5	US	PRIMI	35	3,6,8,	6	1	7.9	2.6	5.3	90	52	278
4	SARASWATHY	30	29136	3	S	G2P1L1	38	2,3,5,	10	1,3	12.1	10.1	2	422	410	230
5	JAYANTHI	21	30655	5	US	PRIMI	35	2,3,5	5	1	6.5	3.5	3	298	202	397
6	RAMANI	27	31900	5	US	PRIMI	39	1,3,4,7,	3	1	8.4	6.2	2.2	206	194	457
7	RANI	28	32217	4	S	PRIMI	30	3,7,9,	1	1,5	2.1	1.1	1	392	354	722
8	MANIMOZHI	33	22750	5	US	G3P1L1A1	37	3,4,9	10	1,4,5	5	2.3	2.7	123	146	567
9	SUGANTHI	23	23504	4	US	PRIMI	20	1,3,4,5	12	1	13.2	7.2	6	252	207	352
10	USHA	25	29863	4	US	PRIMI	30	2,4,5	5	1	4.2	2.2	2	45	42	125
11	BHUVANESHWARI	24	30832	5	US	PRIMI	34	1,3,4,5	10	1	9.2	7	2.2	134	108	408
12	LAKSHMI	32	30846	4	US	G2P1L1	39	3,5,6	1	1	3.1	2.5	0.6	135	130	76
13	POONGODI	32	32906	4	US	G2P1L1	37	1,3,4,7	5	1,2	7.8	5.2	2.6	112	102	296
14	KANIMOZHI	23	34108	5	US	PRIMI	35	7,9	2	1	4	2.7	1.3	370	364	82
15	MUTHAMMAL	27	34642	4	US	G2P1L1	27	1,3,5	8	1	10.2	6.2	4	126	115	315
16	MEENAKSHI	30	34496	4	S	PRIMI	34	3,7	10	1	3	2.1	0.9	162	152	101
17	NANDHINI	22	34856	4	US	PRIMI	38	3,6,8	5	1	11	7	4	90	88	250
18	RANI	26	35136	3	US	PRIMI	37	1,3,5	3	1	8	5.2	2.8	112	98	276
19	VALARMATHY	29	28302	5	US	PRIMI	33	3,7	10	1	5.0	8.8	1.2	250	200	400
20	LAKSHMI	30	36972	5	US	G2A1	26	1,2,3,4,5	7	1,3	12	7	5	120	100	250
21	GANGA	28	37242	4	US	PRIMI	38	1,3,4,5	10	1	10	8.1	1.9	312	290	192
22	REVATHY	24	37991	4	US	PRIMI	35	1,3,4	3	1	6	4.1	2.9	275	260	472
23	MAHESWARI	19	36814	5	US	PRIMI	32	7,9	9	1	2.8	1.7	1.1	154	148	102
24	NEELAVATHY	21	372	5	US	G4A4	38	2,3,4	10	1,3	9.2	5.1	4.1	70	65	272
25	GEETHA	29	1293	4	S	PRIMI	27	4,7,9	2	1,4,5	3	1.2	1.8	104	100	700

26	ANITHA	24	2163	5	US	G2P1L1	40	1,3,4,5	4	1	9.2	5.2	4.0	387	356	112
27	SUMITHRA	19	2089	5	US	G2A1	38	2,3,4	3	1	6.2	4.2	2.0	216	174	256
28	ASHA	20	3628	5	US	PRIMI	37	1,3,4,5	7	1,3	7.2	4.2	3.0	612	596	250
29	MANOMANI	28	4167	4	US	PRIMI	3.7	2,3	3	1	5.0	3.0	2	42	40	112
30	SATHYA	19	4231	4	US	PRIMI	3.7	2,3,4,5	10	1	6	4.2	1.8	286	283	110
31	SARASWATHY	32	5053	5	US	G3A2	27	1,2,3,5	4	1,3	11.2	7.2	4	256	222	352
32	JAYAKODI	26	3492	5	US	G2P1L1	34	2,3,4,7	12	1	14	9.2	4.8	450	400	750
33	JOTHIMADURI	24	1470	4	S	G2P1L1	26	3,7,9	3	1	4	2.8	1.2	192	190	162
34	LAKSHMI	35	37598	4	US	PRIMI	9	7,2,7,	3	1	3	1.2	1.8	96	90	184
35	KUPPU	25	8990	5	US	G2A1	30	3,4,7,9	10	1,4,5	5	4.2	0.8	154	146	300
36	DEEPA	19	10414	4	S	G2P1L1	36	2,3,4,7	15		16	9.2	6.2	490	480	850
37	SYED BEEVI	19	14081	4	US	PRIMI	37	2,3,4,7	3	1,3	12.5	9	3.5	422	382	562
38	RADHA	27	14190	5	US	G2P1L1	26	1,4,5,7	10	1,3	5	2.7	2.3	156	152	140
39	PUNITHA	24	16657	4	US	G4P3L2	39	1,2,3	2	1	8	5.5	2.5	201	196	352
40	REVATHY	28	17345	5	US	G2P1L1	38	1,3,4,5	12	1	6.8	5.4	1.2	318	236	386
41	CHITHRA	29	17477	5	US	PRIMI	39	3,6,8	9	1,2	16.6	10	0.6	38	48	272
42	BAKYALAKSHMI	20	19650	4	US	PRIMI	26	1,2,3,5	10	1,3	11.2	6.2	5	198	102	356
43	KELIDEVI	28	19674	5	US	G3P1L1A1	31	3,7	3	1	6	4.1	1.9	304	381	174
44	REKHA	21	21739	4	US	PRIMI	33	2,6,8	7	1	9.2	5.2	4	297	280	412
45	JEEVA	23	15325	5	US	PRIMI	38	4,7,9	6	1,4	6.2	4.1	2.1	100	97	192
46	MEERA	26	24211	5	US	PRIMI	34	1,4,5,7	5	1	6.8	3.8	3	340	308	432
47	SUMATHY	29	12542	4	US	G2P1L1	36	1,3,5,7	11	1,3	15.1	9.2	5.9	320	311	740
48	SIVARANJINI	20	13621	3	US	PRIMI	37	1,3,5,7	5	1	12	7	5	562	540	823
49	POONGODI	28	18254	4	VS	G2P1L1	37	1,3,5,7	7	1	16	12	4	570	479	875
50	LEELA	34	20127	3	S	G2P1L1	9	3	10	1	5	4.1	0.9	45	42	105
51	PACHIYAMMAL	22	24581	5	US	G2P1L1	37	1,5,7	5	1	7	3.2	3.8	86	84	212

S.NO	PLT	URINE ALB	BS/BP	LEPTO	VIRAL MARKERS	MODE OF DELIVERY	COMPLICATION	BLOOD	FFB	RECOVERY DEATH	BABY OUTCOME	SEX	MATURITY	WT	APGAR <7	DIAGNOSIS
1	2.1	-	+	-	IGM ANTI HEV	NVD	-			R	ALIVE	F	PT	1.9	YES	HEPATITIS E
2	2.2	-	+	-	HBS AG	LSCS	-		2	R	ALIVE	F	T	2.9	NO	HEPATITIS B
3	2.1	-	+	-		NVD				R	I Alive-Dead IIAlive-Dead	F	PT PT	1.3 1.2	YES	IHP
4	1.8		+	-	IGM ANTI HEV	NVD	PPH	3	8	R	DEAD	F	T	3	NO	HEPATITIS E
5	2.0	-	+	-	IGM ANTI HAV	NVD				R	ALIVE	M	PT	2.8	YES	HEPATITIS A
6	2	-	+	-	HBS AG	**OUTLET FORCEPS**				R	ALIVE	F	T	2.9	NO	HEPATITIS B
7	0.8		+			NVD	ABRUPTION			R	DEAD	F	PT	1.5	NO	HELLP
8	2.1		-	-	-	LSCS				R	ALIVE	M	T	2.9	NO	CLD/PHT
9	1.9	-	+		IGM ANTI HEV						DISCHARGED, LOST FOLLOW UP				NO	HEPATITIS E
10	1.8	-	+	+	-	NVD	HEPATAORENAL			R	DEAD	F	PT	1.2	NO	LEPTOSPTROSIS
11	1.7	-	+	-	IGM ANTI HEV	**ASSISTED BREECH**			5	R	DEAD	B	PT	1.3	NO	HEPATITIS E
12	1.6	-	-	-	-	NVD		2		R	ALIVE	B	T	3.3	NO	TRANFUSION REACTION
13	2.1		+	-	HBS AG	LSCS				R	ALIVE	F	T	3	NO	HEPATITIS B
14	1.3	3+	+	-	-	NVD	ABRUPTION	2	10	R	DEAD	F	PT	2.1	NO	HELLP
15	2		+		IGM ANTI HEV	NVD					Alive -Dead	F	PT	1.2	YES	HEPATITIS E
16	0.9	2+	+	-	-	LSCS	DIVC	2	12	R	ALIVE	B	PT	2.1	NO	HELLP
17	2.2	-	+	-	-	LSCS			2	R	ALIVE	F	T	3	NO	IHP
18	2		+			LSCS				R	ALIVE	M	T	2.5	NO	HEPATITIS B
19	0.5	3+	+	-	-	NVD	DIVC	6	20	DEATH	DEAD	F	PT	1.2	NO	HELLP
20	2		+	-							DISCHARGED, LOST FOLLOW UP				NO	UNDETECTED
21	2.1	-	+	-	HBS AG	LSCS	PPH	4	2	R	ALIVE	M	T	3.1	NO	HEPATITIS B
22	2	-	+			NVD					ALIVE	F	PT	2.7	NO	HEPATITIS E
23	1.1	2+	+	-	-	NVD			4	R	ALIVE	F	PT	2.2	NO	HELLP
24	2.1	-	+	-		NVD			3	R	ALIVE	B	T	3	NO	HEPATITIS E
25	1.2	-	+	-	-		OESOPHAGEAL VARICES	6	2	DEATH	-	-			NO	CIRRHOSIS/ PHT

26	2		+		IGM IANTI HEV	NVD				R	ALIVE	B	T	2.5	NO	HEPATITIS E
27	1.9		+			NVD				R	ALIVE	B	T	2.9	NO	HEPATITIS A
28	2		+		IGM ANTI HEV	NVD	PPH	4	8	R	ALIVE	B	T	2.4	NO	HEPATITIS E
29	2		+			NVD				R	ALIVE	G	T	2.3	YES	UNDETECTED
30	2		+	-	HBS AG	NVD				R	ALIVE	G	T	2.9	NO	HEPATITIS E
31	1.5	1+	+	-		NVD				R	DEAD	G	PT	1	NO	HEPATITIS B
32	2		+	-		**OUTLET FORCEPS**	HEPATIC ENCEPHALOPATHY	2	10	R	ALIVE	B	PT	2.1	NO	AFLP
33	0.8	2+	+	-		NVD	ABRUPTION	1	4		DEAD	G	PT	1.2	NO	HELLP
34	1.8	-	+	-	-						DISCHARGED, LOST FOLLOW UP				NO	HYPEREMESIS
35	1.7	-	+	-	-	NVD		2	6	R	DEAD	B	PT	2.2	NO	CIRRHOSIS/ PHT
36	1.0	-	+	-	HBS AG	NVD	HEPATIC ENCEPHALOPATHY	1	10	R	ALIVE	B	PT	2.3	YES	HEPATITIS B
37	0.9	-	+	-	-	NVD	DIVC	4	14	E	ALIVE	B	T	3	NO	AFLP
38	1.2	-	+	+		-	-	-	-	R					NO	LEPTO SPIROSIS
39	2.1	-	+	-	IGM ANTI HBV	NVD	-	2	4	R	ALIVE	B	T	3.2	NO	HEPATITIS B
40	1.5	-	+	-	HBS AG	NVD	-	-	6	R	ALIVE	G	T	2.6	NO	HEPATITIS B
41	2.5	-	+		-	LSCS	-		4	R	ALIVE	B	T	3.8	NO	IHP
42	1.9	-	+	-	HBS AG	-	-		-		DISCHARGED, LOST FOLLOW UP				NO	HEPATITIS B
43	1.2	2+	+	-	-	NVD	CHRONIC HT	1	10	R	Alive-Dead	G	PT	1.4	YES	HELLP
44	2.1	-	+	-	-	NVD	HEPATORENAL	-	4	R	ALIVE	B	PT	1.6	YES	AFLP
45	2.1	-	-	-	-	LSCS	OESOPHAGEAL VARICEAS	1	4	R	ALIVE	B	T	3.1	NO	PORTAL VEIN THROMBOSIS
46	0.8	-	+		-	NVD	HEPATIC ENCEPHALOPATHY			DEATH	DEAD	G	PT	2.3	NO	AFLP
47	1.6	-	+	-	IGM ANTI HEV	NVD		2	8	R	DEAD	G	PT	2.6	NO	HEPATITIS E
48	1.8	-	+	-	HBS AG	NVD		1	8	R	DEAD	G	T	2.8	NO	HEPATITIS B
49	1.9	-	+	-	IGM ANTI HEV	LSCS	HEPATIC ENCEPHALOPATHY	2	8	R	ALIVE	B	T	3.1	NO	HEPATITIS E
50	1.2	-	-	-		ABORTION		2		R					NO	HERE.SPHEROCYTOSIS
51	2.1	-	+	-	IGM ANTI HAV	LSCS	PPH	4	4	R	ALIVE	G	T	3	NO	HEPATITIS A

KEY TO MASTER CHART

SYMPTOMS

1 NAUSEA
2 VOMITING
3 HIGH COLOURED URINE
4 LOSS OF APETITE
5 FEVER
6 ITCHING
7 ABDOMINAL PAIN
8 CLAY STOOLS
9 ABDOMINAL DISTENTION

SIGNS

1 JAUNDICE
2 SCRATCH MARKS
3 HEPATOMEGALY
4 SPLENOMEGALY
5 ASCITES

ABBREVIATIONS

OH	-	Obstetric History
WOG	-	Weeks of gestation
NVD	-	Normal Vaginal delivery
DIVC	-	Disseminated Intravascular Coagulation
IHP	-	Intrahepatic cholestasis of Pregnancy
AFLP	-	Acute fatty liver of Pregnancy
CLD	-	Chronic liver disease
PHT	-	Portal hypertension
PPH	-	Post partum Hemorrhage